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GENESIS OF INTRACELLULAR PIGMENT IN THE SPINAL GANGLIA OF SENILE RATS. AN ELECTRON MICROSCOPE STUDY

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Perhaps the most reliable morphologic correlate of aging in the nervous system that has yet been described is the accumulation of pigment within neurons (10, 13, 15). Although a considerable effort has been made, especially by recent workers, to characterize this material chemically relatively little is actually known. Evidence exists to suggest a relation with both ceroids (14) and pterins (11).

The significance of pigment (lipofuscin) to the physiology of the neuron and the mechanism by which it is formed intracellularly are, as yet, poorly understood. Implicated in the histogenesis of this pigment have been the nucleus (5), the Golgi apparatus (7), and the mitochrondia (9).

It, therefore, seemed advisable to begin our study of the submicroscopic morphology of the aging nervous system with an electron microscope investigation of lipofuscin, the so-called senility pigment. Relative to the genesis of this pigment, data will be presented which, it is believed, contraindicate a mitochrondrial origin.

MATERIAL AND METHODS

Sprague Dawley rats from the colony of the Section on Aging of the National Institute of Mental Health have been utilized throughout this study. The second cervical spinal ganglia of 3 young (age 2 months) females and 3 old females (2 age 24 months and 1 age 25 months) were chosen for electron microscopic study. The rats were stunned by a sharp blow to the back of the neck and killed by opening the thorax and severing the major vessels. The spinal ganglia were dissected free with the aid of a dissecting microscope, cut into small pieces, about 0.5 mm. on a side, and fixed in veronal-buffered osmium tetroxide (pH 7.3) for one hour at room temperature. The tissues were then washed in distilled water, dehydrated in a graded series of alcohol, gradually infiltrated in methacrylate and embedded in methacrylate (3% methyl methacrylate in n-butyl methacrylate). Ultra-thin sections were cut with knives by means of an Ultramicrotome,* mounted on formvar-covered copper grids, and viewed in a Philips EM-75 electron microscope (rated resolution 75 A). Electron micrographs were made on Adox KB-14 35 mm. film which was developed in Microdol.

To compare the distribution of pigment as seen in the light microscope with that seen in the electron microscope, a thick section was made of the methacrylate embedded tissue, mounted on a glass slide in glycerin, and viewed in phase-contrast with an oil immersion lens. Without removing the block from the Ultramicrotome, a thin section was then prepared and viewed in the electron microscope. Photomicrographs were taken on Isopan film, which was developed in DK-50.

Finally, homogenates were prepared from the whole brains of young and old rats in ice-cold 0.25 M sucrose. These homogenates were centrifuged at 10,000 × G. for 2 minutes (0 C.) to remove nuclei and intact cells. The super-

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* Developmental Products Co.

natant fluid was pipetted off and centrifuged again at 29,000 × G. for 20 minutes (0 C.). The resulting fraction is not morphologically pure but contains chiefly mitochondria (with about 10% contamination) which have been found to possess high enzymatic activity (6).*

Samples of these particulate preparations were fixed in cold, veronal-buffered osmium tetroxide, embedded in methacrylate, sectioned, and viewed with the Philips EM-75 electron microscope.

RESULTS

The distribution of dense pigment in the neurons of the spinal ganglion is variable. In both photomicrographs and electron micrographs it is not unusual to find some cells with no visible pigment. Because of the extremely thin sections employed in electron microscopy, it is not possible to say with certainty that neurons containing no pigment exist in the spinal ganglia of old rats. This, however, seems to be the case.

In photomicrographs of both osmium-fixed and frozen-dried spinal ganglia stained with Sudan Black B or Nile Blue Sulphate (12), identifiable pigment has not been observed extracellularly. In electron micrographs dense pigment-like material does occasionally occur extracellularly, chiefly in the fine blood vessels coursing in close proximity to the neuron. It is not possible, however, in osmium-fixed and "stained" specimens, to state that this is the same dense, granular material found intracellularly. It is hoped that the use of frozen-dried specimens, with which one can take advantage of the intrinsic density of the pigment, will clarify this point.

In frozen-dried, paraffin embedded material (fig. 1) and in specimens fixed and "stained" in osmium textroxide and embedded in methacrylate (fig. 2), the pigment is granular in all cases. In the osmium-fixed specimens, especilly when observed in phase-contrast the pigment, as Andrew (1) has reported, often presents a vacuolar structure, a dense peripheral surrounding a less dense central part. The dense pigment particulates occur in various positions within the cytoplasm, sometimes concentrated in a small, circumscribed area usually at one pole of the nucleus and sometimes randomly distributed.

Dense, granular bodies, observed in the electronmicrographs, had a distribution similar to that of the pigment described with the light microscope. By studying alternate thick and thin sections of the same block with the phase-contrast and electron microscopes, it was possible to demonstrate that the pigment observed with the light microscope (fig. 2) is identical to the dense granules observed in the electron microscope at low magnifications (fig. 3). Also, it could be readily ascertained, as it has been found by Hess (9), that the pigment is associated with a vacuolar component of the cytoplasm (figs. 4, 5, 6).

At higher initial magnifications with the electron microscope it was possible to define more clearly the relation between the pigment, which was always found to comprise a dense mass composed of numerous dense granules, and the vacuolar cytoplasmic component with which it is associated. Often the pigment would appear as dense, relatively isolated particulate bodies about 0.5 μ in diameter, which showed no noticeable association with a vacuolar component or, for that matter, with any other cytoplasmic component. Such dense granules were found occurring in groups or alone in various places of the cytoplasm. Pigment configurations were also found which corresponded to the description of Hess (9). These were associated with a large vacuole, of low electron density (fig. 5). In all cases such pigment was found outside the vacuole, separated from it by a clearly defined, intact membrane-like structure. Often the large pigment-associated vacuole was found not to be a simple empty structure, but a configuration consisting of several small vacuoles. In all of these instances, an intact single "membrane" delimited the large vacuole. Such vacuoles bear no obvious relation to mitochrondria, i.e., no typical, internal mitochrondrial structure could be found.

Another configuration often found in these preparations also involved pigment with a vacuolar cytoplasmic component. In this case the large pigment-associated vacuole often, but not always, was characterized by its unusually large diameter (up to about 1 μ) and its dense, thick periphery (fig. 6). Here again, the large vacuole was bounded by a distinct "membrane." In the cytoplasm immediately adjacent to these vacuoles a vesicular component could be seen. In some cases these small vesicles seemed larger than usual and possessed enlarged, dense walls. In other cases the vesicular component was re-

* These particulate fractions were kindly prepared by Joel Garbus of the Section on Aging, National Institute of Mental Health.

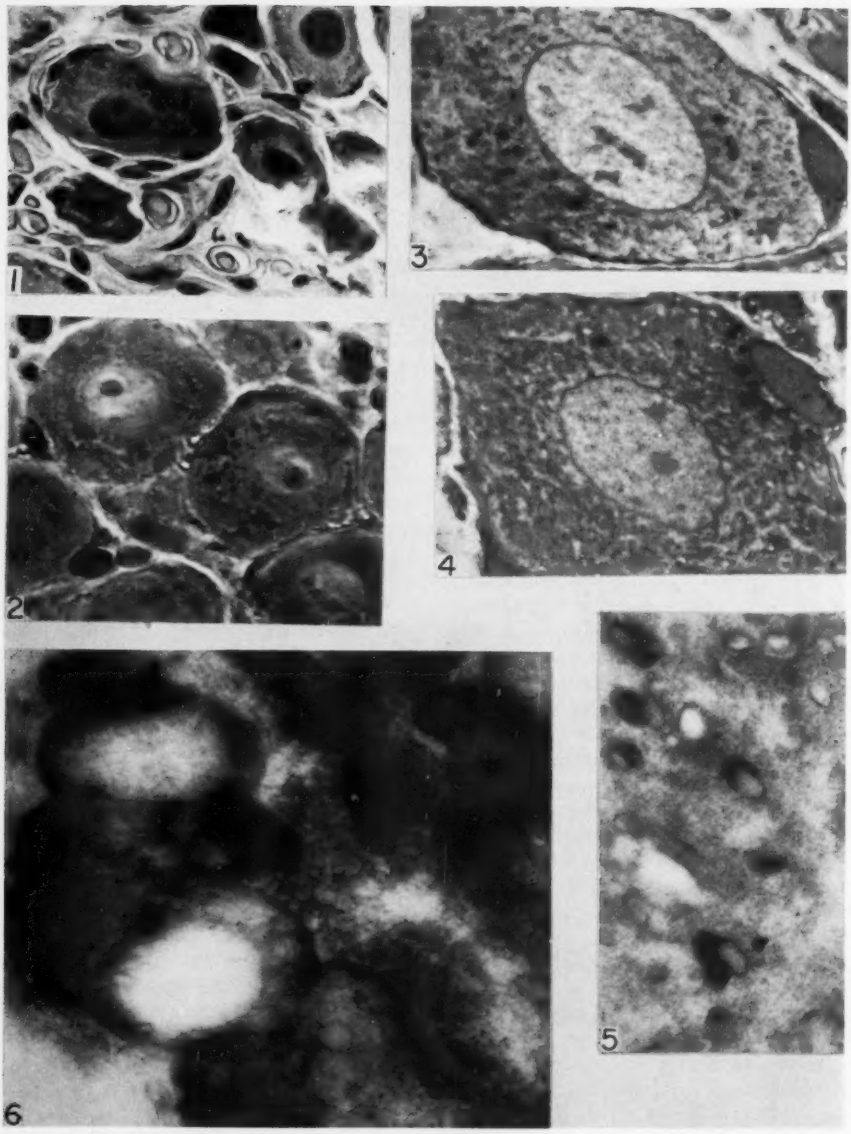

Fig. 1. Photomicrograph of neurons from spinal ganglion of a 24-month-old rat, fixed by freezing and drying, and stained with Sudan Black B. × 1,060.

Fig. 2. Phase contrast, photomicrograph of neurons from spinal ganglion of a 24-month-old rat fixed with veronal-buffered osmium tetroxide and embedded in methacrylate. × 1,050.

Fig. 3. Electron micrograph of a neuron from the spinal ganglion of a 24-month-old rat fixed with osmium tetroxide. × 2,900.

Fig. 4. Electron micrograph of a neuron from the spinal ganglion of a 24-month-old rat fixed with osmium tetroxide. Pigment associated with a vacuolar cytoplasmic component is seen in peripheral portion of cell. × 2,900.

Fig. 5. Electron micrograph demonstrating pigment-associated vacuoles in close proximity to Golgi complex. × 23,800.

Fig. 6. Electron micrograph demonstrating details of pigment and pigment-associated vacuoles. (Philips EM-100B). × 55,000.

placed by small dense granules, similar in size to the vesicles (about 300 Å – 400 Å in diameter) and it was not uncommon to find all these configurations, i.e., vesicles, granules, enlarged vesicles with dense walls, associated with the same large vacuole.

One other pigment or pigment-like formation was commonly observed. Not in obvious association with any vacuolar component, nor with intact and identifiable mitochondria, were dense, rounded bodies containing denser internal granules and sometimes also small vesicles of a diameter similar to that of the dense granules.

Electron microscopic examination of the particulate fractions revealed that although morphology was poor, mitochondria could be readily identified in fractions from both young and old animals. Neither pigment-vacuole formations nor dense bodies, morphologically similar to the pigment observed in sections, could be identified in these fractions.

DISCUSSION

Electron dense (osmiophilic) configurations have been described in the cytoplasm of old neurons fixed and "stained" with osmium tetroxide and viewed with the electron microscope. The similarity between this material, which is distinctly particulate, and the granular pigment (lipofuscin) observed with the light microscope in both phase-contrast and in stained preparations, has been demonstrated. The term pigment, however, is perhaps inaccurate, especially when referring to electron micrographs, for rigid definition requires the presence of color. With the electron microscope contrast results from the differential scatter of electrons by a structure relative to that of its background. This is a function of density, and color, therefore, is not involved in image formation. A particle could seem dense in electron micrographs and not, in a strict sense, be pigment but perhaps a pigment precursor. The granular structures referred to in this report as pigment are electron dense, are not observed in young control specimens, and have an intracellular position corresponding to that of pigment as demonstrated with the light micoscope. It remains to discuss the derivation of this very conspicuous cytoplasmic inclusion.

The electron micrographs presented here and those of Hess (9), indicate a morphologic relation between these dense granular structures and a vacuolar component of the cytoplasm. These vacuoles have been described as resulting from degenerate mitochrondria, and thus Hess has proposed a mitochondrial origin of the senility pigment.

It is, of course, difficult to determine the nature of the cytoplasmic vacuoles found in association with pigment. They may bear a striking resemblance to the inclusions described by Dempsey (4) in the cells of the choroid plexus of rats fed silver nitrate and interpreted by him as degenerate mitochondria. However, a mitochrondrial origin of the senility pigment, such as the mechanism proposed by Hess (9), cannot explain the results obtained here. In the first place, the pigment-associated vacuole is limited by a single, clearly defined, "membrane" and not the double membrane characteristic of mitochondria. Secondly, this single "membrane" is usually found to be intact between the pigment and the vacuole. If the mitochondria were to vacuolate, and the vacuoles coalesce to form pigment, as proposed by Hess, one would expect pigment inside the vacuole "membrane." If, in the case of those vacuolar structures with thickened, dense walls, the smaller vacuoles (or vesicles) which form within the periphery of the vacuole were to coalesce to form pigment, one would again expect to find the pigment granules within the confines of this limiting vacuole "membrane." Such does not seem to be the case.

Additional evidence in support of the thesis that the pigment-associated vacuoles are not of mitochondrial origin has been obtained from the electron microscope study of mitochondrial fractions. Because of the relatively dense nature of the pigment (11), one might not expect to find large pigment deposits in mitochondrial fractions, including the morphologically impure particulate fractions employed in this study. However, because of the impure nature of the fractions it does not seem unreasonable to expect to find at least some of the various forms of vacuoles which have been described and which, in sections, are associated with pigment. This, of course, assumes that such vacuoles would retain their morphologic integrity during the fractionating procedure and that they are, at least in density, similar to the mitochondria. As it has been stated, such vacuolar configurations were not observed in the fractions from either young or old animals.

We are, therefore, left with two alternative possibilities: 1) that the mitochondria are indeed intimately associated with the process of pigment formation but that the formation of intramitochondrial vacuoles and vesicles does not play a direct role in the mechanism, the formation of pigment thereby taking place at the surfaces of mitochrondria within the juxtamitochrondrial cytoplasm; or 2) that the large vacuoles, morphologically related to pigment particulates, are not related to mitochondria. The data presented here seem to favor the latter view, i.e., that mitochrondria are not directly related to the mechanism whereby pigment is formed in senile nerve cells.

If the latter supposition is correct, pigment formation could be expected to take place within the cytoplasm of senile neurons, unrelated to any particular cytoplasmic organelle and only morphologically related to the vacuoles. On the other hand, it seems justifiable to relate these pigment-associated vacuoles, and thereby the process of pigment formation, with a cytoplasmic organelle other than the mitochondria.

For the purpose of this discussion it does not seem necessary to enter the current controversy concerned with the reality of the Golgi apparatus. Suffice it to say that a morphologic relation between the Golgi apparatus and senile pigment has been demonstrated by the light microscopic studies of Gatenby (7, 8). The submicroscopic morphology of this specifically differentiated cytoplasmic locus has been investigated by Dalton and Felix (2, 3) whose electron microscope studies show it to be a complex structural entity composed of vesicles, vacuoles, membranes, and membrane-associated particulates.

In figure 6, it is seen that the pigment-associated vacuoles bear a resemblance to the Golgi complex of Dalton and Felix (2, 3). Associated with their peripheries are small vesicles and membranes, and it therefore seems reasonable to relate these pigment-associated vacuoles and the immediately surrounding cytoplasm with the Golgi complex.

That the senility pigment derives from the Golgi apparatus has been proposed by Gatenby (7). The mechanism which Gatenby proposed for the histogenesis of pigment, however, differs from that suggested by the electron micographs presented here. There has been no indication in the present investigation that the Golgi apparatus fragments (1, 7) or that the fragmented parts transform into pigment and move through the cytoplasm to their final locus, as proposed by Gatenby (7).

Consideration of the electron micrographs leads one to suggest the following mechanism for the genesis of senile pigment: 1) the walls of vesicles and vacuoles of the Golgi complex thicken; in the latter, smaller vesicles form and undergo a similar thickening of their walls; 2) the vesicle walls continue to thicken and the vesicles become particulate; 3) these particulates coalesce, forming larger particular complexes. That the pigment particles, during any or all of these suggested formative stages, may move through the cytoplasm seems plausible but evidence does not exist in this study to either support or refute such movement.

The above mechanism has been derived from interpretation of electron micrographs and is presented only as a suggested course of pigment derivation.

SUMMARY

Intracellular pigment, identical with that observed with the light microscope, has been observed in electron micrographs of osmium-fixed neurons from spinal ganglia of senile rats.

Evidence, based on these electron micrographs, has been presented which tends to disclaim the contention that senility pigment (lipofuscin) originates from degenerate mitochondria.

It is suggested that the Golgi complex, as described by Dalton and Felix, is associated with the derivation of this pigment and a mechanism for its formation is proposed.

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GROWTH, DISEASE, AND AGING IN THE RAT*

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The study of aging in man is difficult because of the lack of genetic and environmental control. In the rat these factors can be controlled and the findings in animals can supply information and valuable clues to human gerontology. On this premise our rat colony was established more than 10 years ago and over 50 generations of inbred animals have been raised under conditions particularly favorable for long survival.

In connection with our studies on aging it seemed advisable to extend our observations so as to include studies on growth in relation to longevity and senescence. Accordingly data on body weight, body length, and tibia length were obtained under carefully controlled conditions in rats from weaning through maturity and old age. Parallel studies on the histology of the proximal tibial epiphysis were also made to determine whether epiphyseal non-union, a phenomenon peculiar to the rat, was significant with respect to potential growth in old animals. These findings together with observations on the influence of chronic disease on growth are described in the present paper.

Lung infection is endemic and is the major cause of death in most rat colonies. The disease seriously affects the validity of experimental results and especially hampers studies on growth and longevity. By a process of elimination and selection described later, pulmonary infection has been largely excluded from our colony so that data have been derived wholly from animals with uninfected lungs. Mortality has been due entirely to other diseases.

Rat Selection.—Data were obtained from a total of 858 Sprague-Dawley rats, 543 males and 315 females. Details as to numbers at different age levels and as to health status are given in tables 1-4. The animals fell into 2 categories. The first consisted of 133 males and 138 females which continued to gain weight until they were sacrificed (tables 1 and 2). These rats showed at autopsy no discernible gross or microscopic lesions. Up to about 170 days, random choice was employed since the incidence of lesions until this age was negligible. Later, when pathologic changes began to appear, selection became necessary and with advancing age it was used to a greater and greater extent as the frequency of lesions increased. After 681 days in males and after 801 days in females, the number of disease-free animals was too small to obtain significant mean values for further growth studies. Since tissue sampling was restricted to relatively small sections of organs, it is possible that some rats classified as free from lesions actually had undetected lesions. In such cases, however, the changes were not far enough advanced to interfere with steady weight gain.

The second category comprised 410 males and 177 females; all had lesions of moderate or marked severity and had lost weight. Most of these animals were over 700 days old but some, especially males, were younger (tables 3 and 4). No selection was made in this category, excepting a small number of animals with pulmonary infection which were excluded.

In the study by Simms and Berg (4) on the accumulation and progression of lesions in relation to age, all of the data were based on findings in rats chosen at random. The present investigation differed in that after the onset of disease, selection was employed in order to obtain data on animals free from lesions. In both studies classification of lesions according to type and severity was the same.

Colony Conditions.—The rats were raised in air-conditioned quarters at constant temperature and humidity and with regulated 12-hour periods of light and darkness. The diet consisted of Rockland "D free" pellets, replenished biweekly and fed ad lib. Fertility was excellent on this diet. Mating was restricted to animals used only for breeding and the females were discarded after bearing 3 litters. Animals were weaned at 4 weeks of age and a suitable number of young were chosen at random for the colony. As a rule a single cage held 4 rats. A

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TABLE 1. MEASUREMENTS OF MALE RATS FREE FROM LESIONS.

Age (Days)		Tibia Length (cm.)				Body Length (cm.)				Body Weight (Gm.)		
Mean	Range	No.	Mean	S. D.	Range	No.	Mean	S. D.	Range	No.	Mean	Range
30	29–32	10	2.37	0.100	2.17–2.53	10	12.4	0.70	11.2–13.3	10	60	45–72
48	46–51	13	3.17	0.110	3.01–3.36					13	154	134–192
67	64–70	15	3.65	0.130	3.44–3.90	15	19.9	0.78	18.3–21.3	15	225	190–263
100	100–100	10	4.13	0.140	3.80–4.25	10	22.5	0.60	21.8–23.5	10	328	298–361
162	157–170	12	4.38	0.056	4.28–4.46	12	23.7	0.30	22.3–24.6	12	380	344–403
242	234–249	10	4.43	0.067	4.30–4.52	10	24.2	0.30	23.8–24.6	10	400	359–423
328	324–334	10	4.50	0.050	4.40–4.58	10	24.7	0.70	23.5–25.6	10	438	386–482
522	517–526	20	4.58	0.077	4.44–4.70	20	24.3	0.50	23.6–25.3	20	486	425–540
622	618–625	15	4.56	0.090	4.40–4.75	15	25.0	0.53	24.4–26.4	15	456	415–506
681	676–687	18	4.61	0.089	4.36–4.73	18	24.8	0.59	24.0–25.7	18	474	416–548
Totals.....		133				120				133		

TABLE 2. MEASUREMENTS OF FEMALE RATS FREE FROM LESIONS.

Age (Days)		Tibia Length (cm.)				Body Length (cm.)				Body Weight (Gm.)		
Mean	Range	No.	Mean	S. D.	Range	No.	Mean	S. D.	Range	No.	Mean	Range
31	29–32	10	2.31	0.166	2.09–2.58	9	12.3	0.70	11.3–13.3	10	58	42–76
51	49–52	14	3.21	0.080	3.10–3.42					14	145	120–184
71	67–74	10	3.41	0.093	3.30–3.58	10	18.2	0.53	17.1–19.0	10	155	135–170
79	79–79	6	3.57	0.044	3.50–3.63	6	18.5	0.21	18.3–18.8	6	178	170–184
108	107–109	11	3.74	0.040	3.68–3.80	11	19.5	0.50	18.8–20.5	11	192	172–217
176	175–180	10	3.90	0.042	3.81–3.96	10	20.1	0.37	19.5–20.7	10	220	201–239
357	316–391	26	3.93	0.058	3.81–4.06	26	20.2	0.48	19.1–21.0	26	238	200–271
585	567–594	14	3.96	0.088	3.82–4.09	14	19.8	0.74	18.6–21.0	14	271	238–306
801	763–813	37	3.99	0.086	3.81–4.19	36	21.2	0.50	20.4–22.4	33	279	218–340
Totals.....		138				122				134		

quiet atmosphere, gentle handling, and avoidance of stresses were emphasized in the management of the colony.

Control of Pulmonary Infection.—Floors, walls, and attendants' uniforms and gloves were kept clean; dust from pellets was sifted and discarded. Cages and water bottles were sterilized at regular intervals. Visitors were kept at a minimum and were required to wear gowns.

The program to control lung infection was started 6 years ago and initially all rats with the following signs or symptoms were removed from the colony: 1) bloody nasal discharge; 2) rapid, labored respiration; 3) rhonchi due to sticky tracheobronchial secretions; 4) male rats up to 550 days old and females up to 750 days old having no obvious respiratory symptoms but either failing to gain weight or losing weight. The symptom-free survivors were watched closely for evidence of early lung involvement and such rats were promptly eliminated. Particularly important was the removal of infected breeders. Rigorous adherence to this regime reduced the incidence of chronic and acute lung infection from an over-all figure of more than 50 per cent to 2 per cent for the chronic type and to 4 per cent for the acute type. This low incidence has been maintained for the past 5 years. The chronic form is characterized by suppurative bronchiectases, bronchiectatic abscesses, and pneumonitis. The acute type is a fulminating, rapidly fatal, hemorrhagic, necrotizing pneumonitis, often with abscess formation. None of the animals included in this study had infected lungs.

Histologic Examinations.—Apparently healthy animals used to establish growth curves in the absence of lesions were killed at different ages by intraperitoneal injection of nembutal. The balance of the rats either completed their life span or were killed by nembutal when they were moribund or had hind leg paralysis (2). Complete autopsies were performed immediately after death; animals dying sponta-

TABLE 3. MEASUREMENTS OF MALE RATS HAVING LESIONS.

Age (Days)		Tibia Length (cm.)				Body Length (cm.)				Body Weight (Gm.)		
Mean	Range	No.	Mean	S. D.	Range	No.	Mean	S. D.	Range	No.	Mean	Range
469	417–496	12	4.55	0.096	4.37–4.69	11	23.9	1.10	22.4–26.0	11	366	266–477
579	500–597	34	4.56	0.101	4.36–4.76	23	23.8	1.20	21.0–25.4	32	342	204–560
655	602–699	76	4.57	0.108	4.25–4.83	68	23.8	0.98	21.3–26.5	69	356	206–562
747	700–798	84	4.57	0.113	4.29–4.87	72	23.8	0.96	21.3–26.0	80	337	216–560
854	802–898	86	4.56	0.106	4.34–4.78	81	23.8	0.88	21.2–25.7	80	336	240–510
940	900–998	76	4.55	0.112	4.18–4.78	70	23.9	0.95	21.2–25.8	63	328	207–454
1038	1002–1090	38	4.51	0.120	4.18–4.76	36	23.8	0.73	22.5–25.5	35	314	230–406
1124	1110–1142	4	4.52		4.48–4.57	4	23.8		23.0–24.2	3	294	243–370
Totals.....		410				365				373		

TABLE 4. MEASUREMENTS OF FEMALE RATS HAVING LESIONS.

Age (Days)		Tibia Length (cm.)				Body Length (cm.)				Body Weight (Gm.)		
Mean	Range	No.	Mean	S. D.	Range	No.	Mean	S. D.	Range	No.	Mean	Range
544	501–599	12	3.98	0.060	3.87–4.10	11	20.5	0.73	19.0–21.7	10	240	178–333
643	601–692	15	3.97	0.080	3.87–4.12	14	20.3	0.71	19.1–21.6	14	210	148–268
744	709–796	20	3.98	0.091	3.81–4.20	18	20.6	0.82	18.2–21.7	11	219	168–270
860	805–899	38	3.98	0.097	3.63–4.10	33	20.6	1.03	18.6–24.0	31	234	162–454
952	902–999	38	4.01	0.089	3.78–4.15	30	20.6	0.74	19.7–22.1	31	221	155–320
1051	1003–1098	39	3.97	0.096	3.78–4.14	32	20.6	0.88	18.8–22.3	29	206	174–333
1143	1104–1193	12	3.96	0.070	3.87–4.07	9	20.5	0.74	19.3–21.6	8	224	190–273
1230	1215–1246	3	4.04		3.99–4.11	3	20.9		20.4–21.3	1	272	
Totals.....		177				150				135		

neously were examined before autolysis set in. Specimens were taken from all tissues and after fixation in Zenker's fluid were imbedded in paraffin. Sections were stained with hematoxylin and eosin for histologic study. The proximal epiphysis of the tibia was prepared for examination by preliminary decalcification in a 5 per cent nitric acid solution.

Measurements.—Body weights were terminal values. Tibia length was determined by precision calipers and was the distance between the spines of the tibial head and the medial malleolus. Body length was the calipered measurement from the tip of the nose to the anus.

RESULTS

Body Weight. — Starting at equal weaning weights, increments at corresponding ages were greater in males free from lesions than in females and decreased progressively with advancing age (tables 1, 2 and figs. 1, 2). Weight increases continued to a later age in the female than in the male because disease set in later in the female. Males reached their maximum weights (mean of 486 Gm.) at 522 days and females attained their highest weights (mean of 279 Gm.) at 801 days. The subsequent course of the weight curves followed a plateau and then a decline, a manifestation of advancing disease process. In the younger animals in which lesions had developed sooner there was a corresponding earlier break in the weight curves. Relatively high weights were found in rats with tumors or fluid accumulations but the net values after removal of the tumor or fluid was low. The commonest pathologic conditions occurring in our rat strain were chronic nephrosis and glomerulonephritis, periarteritis, myocardial degeneration and fibrosis, skeletal muscle dystrophy, and certain tumors, viz., adenoma of the anterior lobe of the pituitary, phaeochromocytoma of the adrenal medulla, adenoma of the thyroid, and fibroadenoma of the breast in females.

Body weight increased rapidly up to about 170 days after which the rate of increase diminished sharply. Increments with advancing age are due partly to deposition of fat in the sub-

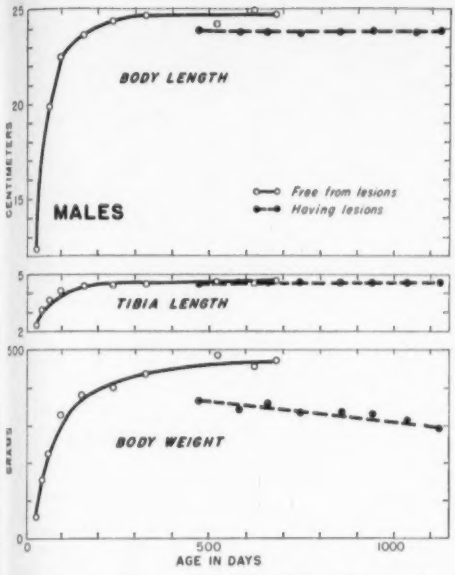

Fig. 1. Curves of body weight, tibia length, and body length in male rats free from lesions, and also in animals having lesions.

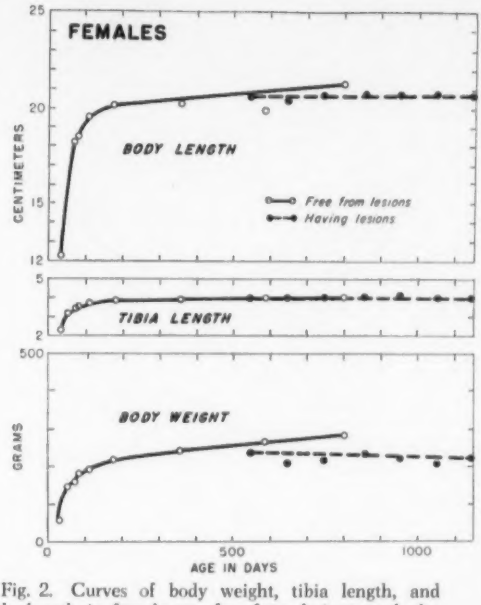

Fig. 2. Curves of body weight, tibia length, and body length in female rats free from lesions, and also in animals having lesions.

cutaneous tissue, in the retroperitoneal and perirenal spaces, in the mesenteries of the spermatic cord, of the ovary, of the uterus, and of the intestine and in the interscapular area. Whether the accumulation of fat in the mature rat can be termed normal is questionable. Zucker and associates (6) have an affirmative opinion based on the finding that rate of fat deposition does not disturb the straight line relation between log body weight plotted against reciprocal of age. Nevertheless the fact remains that fat accumulation is caused by an imbalance between energy requirement and food intake and to this extent is abnormal. Certainly cage confinement restricts spontaneous activity more and more as an animal grows and thus contributes to fat deposition; unlimited food intake furthers it. It is plausible that regulation of food intake according to energy needs will reduce fat formation, will diminish rate and extent of body weight increments, and body weight curves will be nearly flat after 170 days.

Tibia Length—At weaning, although body weights were equal, the tibia was longer in males than in females and continued to grow at a faster rate in males. Between 100 and 681 days in males there was a 12 per cent increment in tibia length while in females the increase from 108 to 801 days was only 7 per cent. Until about 170 days in both sexes rate of growth of the tibia was rapid and then declined abruptly. Later, increments became extremely small but were found to be statistically significant when a sufficient interval elapsed between measurements. For example, in males the P value was 0.001 for the difference between the maximum mean length of 4.61 cm. at 681 days and the mean length of 4.50 cm. at 328 days; for females, the P value was 0.001 in comparing the maximum mean length of 3.99 cm. at 801 days with the mean length of 3.93 cm. at 357 days. Evans and coworkers (1, 5) found no appreciable change in tibia length in female rats after approximately 120 days. After peak tibia length was reached, time intervals of later measurements were too short to ascertain if further statistically significant growth occurred. The lower values for tibia length in male rats over 1,000 days old could be explained on the basis of shrinkage of bone matrix, atrophy of articular cartilage, or osteoporosis. Another explanation could be unintentional selective breeding giving larger animals among the younger age groups.

Of particular interest was the finding that mean tibia lengths were nearly the same in rats

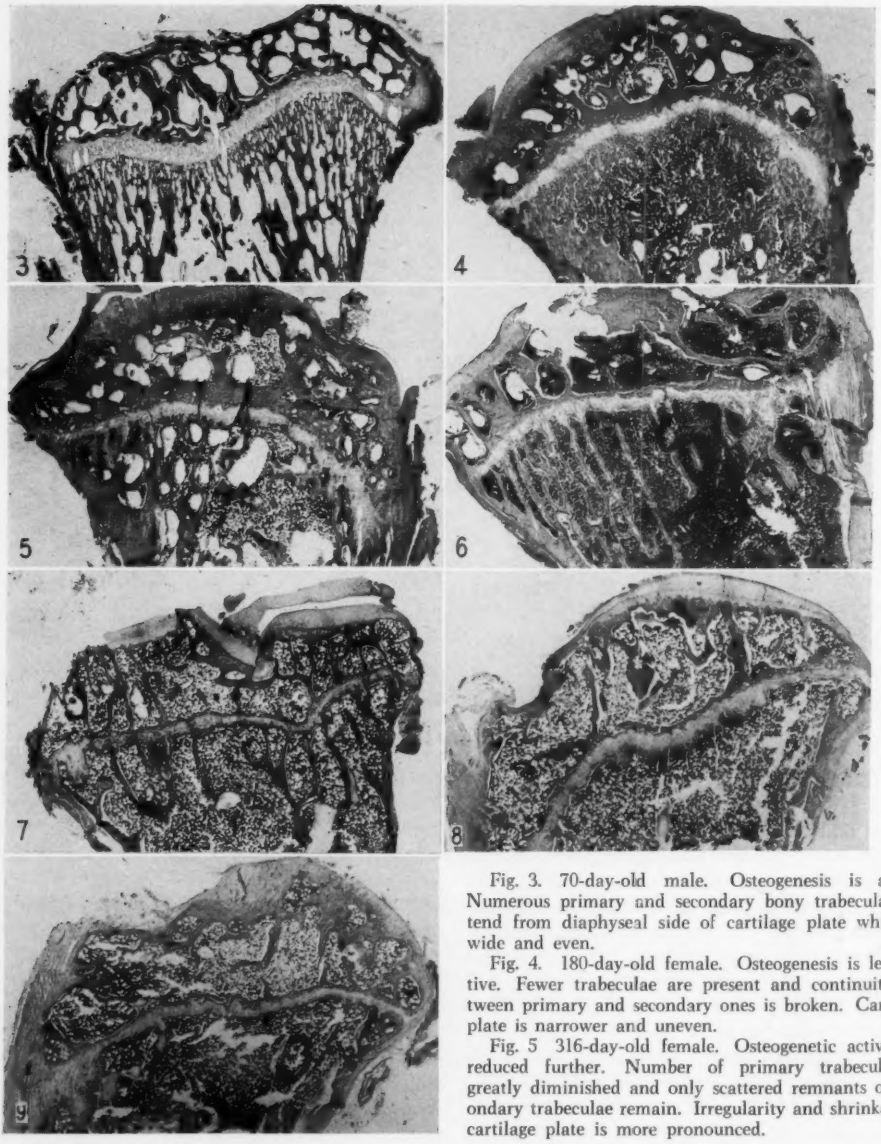

Fig. 3. 70-day-old male. Osteogenesis is active. Numerous primary and secondary bony trabeculae extend from diaphyseal side of cartilage plate which is wide and even.

Fig. 4. 180-day-old female. Osteogenesis is less active. Fewer trabeculae are present and continuity between primary and secondary ones is broken. Cartilage plate is narrower and uneven.

Fig. 5 316-day-old female. Osteogenetic activity is reduced further. Number of primary trabeculae is greatly diminished and only scattered remnants of secondary trabeculae remain. Irregularity and shrinkage of cartilage plate is more pronounced.

Fig. 6. 790-day-old male. Osteogenesis is minimal. Several long, thin trabeculae extend from cartilage plate, which is very irregular.

Fig. 7. 1071-day-old female. No evidence of osteogenesis is present. Disc is reduced to a narrow, irregular band of cartilage enclosed in bony plates to which a few, thick primary trabeculae are attached.

Fig. 8. 1054-day-old male. Disc is relatively wide but uneven. On diaphyseal side of cartilage are blunt ends of trabeculae which have largely disappeared.

Fig. 9. 1133-day-old female. Marked disarrangement and degeneration of cartilage cells. Disc persists but incased in bony plates. A few remnants of trabeculae remain.

Figures 3 through 9 show typical changes, at different ages, in the proximal tibial epiphysis of the rat. All 10X. Hematoxylin eosin.

with advanced lesions and with weight loss as in those free from lesions. For instance, the mean tibia length for males free from lesions was 4.58 cm. at 522 days while in their counterparts with well developed lesions and weight loss, it was 4.56 cm. at 579 days. Similarly in females the tibias of animals free from lesions averaged 3.96 cm. at 585 days as compared to 3.98 cm. at 544 days for those with lesions. In fact, the maximum female tibia measurement of 4.01 cm. was found at 952 days in rats with disease and considerable weight loss.

Body Length. — Rate of increase of body length closely paralleled rate of tibia growth. For males with no detectable lesions a maximum mean body length of 25.0 cm. was found at 622 days; the corresponding value for females was 21.2 cm. at 801 days. In females measurements were about the same in animals with or without lesions but in males body lengths were shorter in those with lesions. This difference was probably due to the greater loss of subcutaneous perineal fat in the male.

The Proximal Tibial Epiphysis.—In general the order of closure of the skeletal epiphyses in the rat is the same as in other mammals (5). Most of the epiphyses in the rat have united by 120 days. However, certain epiphyses fail to close even in old age. At least one epiphysis in each of the major long bones and the epiphyses of the caudal vertebrae are patent into senescence.

In figures 3 to 9 are shown the changes that are found in the proximal tibial epiphysis of rats from 70 days to over 1100 days old. These are presented as typical alterations with advancing age. Some variation in the appearance of the epiphysis is found in old animals, but there is no evidence of osteogenetic activity.

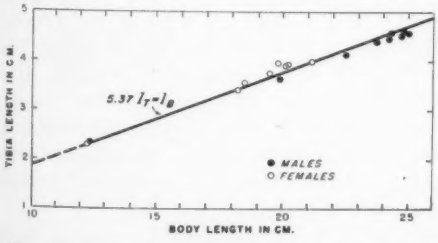

Fig. 10. Plot of tibia length (l_T) against body length (l_B) showing straight line relation of growth rates. Points for males and females fall approximately on the same line passing through the origin and following the indicated equation.

During early life when growth is rapid the cartilage plate of the proximal tibial epiphysis is wide, and numerous long, thin, interlacing, newly formed bony trabeculae are found on the diaphyseal side of the disc. By about 170 days when increments in tibia length diminish markedly there is corresponding histologic evidence of decreased osteogenesis at the epiphysis. The width of the cartilage is decreased, the margins are somewhat irregular, and the number of new trabeculae is reduced. At about 300 days there are further signs of diminishing osteogenesis. Narrowing and irregularity of the cartilage are greater and trabeculae are fewer. With advancing age regressive changes in the epiphysis become more pronounced. The cartilage becomes increasingly narrow and irregular and new bone formation is minimal. In very old rats over 1,000 days of age a zone of cartilage persists but it is incased in bony plates. A few stubby trabeculae remain attached to the disc but there is no evidence of active osteogenesis. In animals over 1100 days old the epiphysis is still open.

Comparative Growth Rates and the Principle of Heterogony

Huxley (3) demonstrated that the ratio of relative growth rates between any 2 parts of the body, or a part of the body and the whole, remains constant. He also showed that the change in the log of organ weight or organ dimensions at a given time is proportional to the change in the log of body weight or body dimensions during the same time. To this relation Huxley applied the term heterogony.

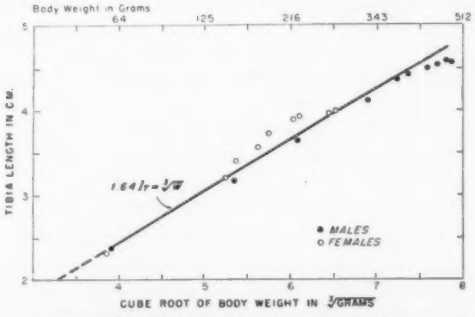

Fig. 11. Plot of tibia length against the cube root of body weight ($\sqrt[3]{W}$) showing straight line relationship. Points for males and females fall approximately on the same line passing through the origin and following the indicated equation.

Applying Huxley's principle to our own material but using linear instead of logarithmic scales, the measurements of male and female rats free from lesions were plotted to determine the relation of tibia length and body length growth rates. The points fall on a relatively straight line common to both sexes, except for a slight downward concavity for higher values in females (fig. 10). When the linear plot is transferred to a logarithmic scale the resultant straight line has the slope of unity and conforms with Huxley's principle of heterogony.

A similar plot of tibia length and cube root of body weight again shows a linear relation with points for both sexes falling on a single line with a slight downward concavity at higher values for females (fig. 11). These data are also consistent with Huxley's principle, and with Zucker and Zucker's finding of a constant relation between femur bone ash weight and body weight (6).

It is of interest that even though males and females have quite different growth rates, the data of both sexes in the 2 graphs fall on one line, demonstrating that both sexes have the same proportionality constant when 2 body dimensions are compared.

DISCUSSION

As a result of controlling lung infection, the average longevity of rats in our colony has been increased considerably, in males to about 750 days, and in females to about 900 days. However, the maximum life span has not been lengthened beyond 1200 days in the male and 1300 days in the female, because the diseases which develop with advancing age, and are the chief causes of death, continue to operate as limiting factors. A similar situation exists in man. With the introduction of new therapeutic agents such as antibiotics and insulin, life expectancy has been increased but the maximum life span has not changed due to the fact that the toll from the so-called degenerative diseases of old age has not been altered.

In the rat, chronic pathologic conditions appear while skeletal growth is going on, but in man chronic disease develops largely after skeletal growth has stopped (the last epiphysis closes at about 20 years of age). Increments in skeletal size continue for about 60 per cent of the rat's life span while in man the period of skeletal growth occupies less than 30 per cent of the life span. The principal lesions found in senescent rats are in the categories of cardiovascular-renal lesions and neoplasms, and they involve the same tissues that are affected in aging man.

On a histologic basis, persistence of certain epiphyseal cartilages in very old rats seems to indicate that skeletal growth has not yet ceased. Our findings support the generally accepted idea that the epiphyseal disc does not unite even in the senescent animal. But the histologic appearance in very old rats is such as to indicate that further measurable growth is very unlikely.

It is a moot question whether or not the pathologic changes occurring in later life are degenerative in the sense that they represent a breakdown of intrinsic biologic systems within tissue cells. Whether or not these changes are inevitable with time is another debatable question. An increased susceptibility to disease has been found with advancing age (4). For a better understanding of the aging process, it would be helpful if we could extend the life span of our experimental animals by preventing or eradicating the diseases that occur in the older animals. An effort in this direction is our present study on muscular dystrophy, the most frequent terminal cause of death of old rats in our colony. The skeletal muscle lesions resemble the changes resulting from experimental vitamin E deficiency (2) and on this basis large doses of alpha tocopherol have been given to a group of rats to determine if the spontaneous muscle disease can be prevented or cured.

The female rat is superior to the male with respect to vigor, to longevity, to resistance to disease, and to length of period of continued growth. Experiments in progress are designed to determine whether these differences are related to the smaller size of the female or to other factors, such as hormones. These studies should also help to elucidate whether maximum growth is optimum growth as considered in relation to susceptibility to disease and to longevity.

SUMMARY

Procedures that have been successful in controlling lung infection in our rat colony have been described. Rates of growth for both sexes, as determined by body weight, body

length, and tibia length have been established under standardized conditions from weaning through maturity and old age. Data are given for animals free from lesions and for animals with chronic disease. Linear plots of tibia length against body length and of tibia length against the cube root of body weight give points for both sexes falling on a straight line. These data are in accord with Huxley's principle of heterogony. Histologic studies of the proximal tibial epiphysis show non-union even in senescence but there is no evidence of continued osteogenesis into old age. These standardized patterns of growth can be used as the basis for comparative studies on the effects of growth retardation in relation to prolongation of the life span.

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SYSTOLIC BLOOD PRESSURE AND HEART RATE IN RELATION TO LUNG DISEASE AND LIFE DURATION IN MALE RATS

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Life insurance companies have made an extensive study of the relation between the level of blood pressure and longevity as an aid in predicting human mortality risks. They find an excessive mortality among hypertensives (6, 8, 12, 20, 22) and a reduced death rate in hypotensives (1, 6, 8, 11, 22, 25).

Heart rate has received little attention in the forecast of life expectancy, although several observers (19, 22) have noted that a low heart rate has a favorable effect on life duration.

The purpose of the present investigation is to determine whether blood pressure and heart rate have a similar prognostic significance in the rat.

MATERIALS AND METHODS

Sixty-eight non-inbred, male albino rats of the Wistar strain were housed in a small air-conditioned room and fed ad libitum on a pelleted diet as described previously (10).

Systolic blood pressure in the caudal artery of the tail was determined under light ether anesthesia, at a temperature of 35 C., using an indirect optical method described by Byrom (4). Systolic blood pressure was diminished during anesthesia but rose again in the recovery phase, reaching a steady level just before the rat became conscious and moved. In most rats this value was reproducible to within 5 mm.Hg in separate estimations on the same day. The mean of 3 to 5 estimations was recorded as the systolic blood pressure. Determinations were made at 2 stages in the life cycle, in young adult life at 340 days and in old age at 675 days.

The heart rate was obtained from the electrocardiogram, which was recorded under light pentobarbital anesthesia, on a General Electric vacuum tube electrocardiograph.

Animals were maintained until natural death and the gross pathology of the lung was studied at autopsy.

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RESULTS

Age Changes.—The systolic blood pressure of 68 young male rats of age 340 ± 0.7* days ranged from 100 to 150 mm. Hg, yielding a mean of 121.0 mm. Hg, with a standard error of 2.2 mm. Hg. In old age at 675 ± 0.6 days,* the systolic pressure of 34 surviving rats ranged from 60 to 155 mm. Hg, giving a mean of 113.8 ± 3.9 mm. Hg.

The heart rate of these rats decreased from 378 ± 4.8* beats per minute at an age of 340 days to 357 ± 8.9* at 675 days.

Systolic Blood Pressure, Heart Rate, and Life Duration.—The data showed a small increase in the systolic blood pressure with life duration, both in observations on young rats (table 1) and on old rats (table 2). In the case of young rats the value of the correlation coefficient was 0.39 ± 0.10. The variation in life duration with systolic blood pressure is shown in a scatter diagram (fig. 1). As in a previous article (10) the relationship was studied by dividing the rats into 4 life duration classes: very short lived (428-600 days) short lived (619-700 days), long lived (704-846 days), and very long lived (857-1084 days). Analysis of variance of the blood pressures of young rats revealed a significant difference between the life duration groups ($F = 4.03$, $P < .05$). The mean systolic blood pressure of the very long lived group was significantly higher than that of the very short lived group ($t = 3.31$, $P < .01$) and that of the short lived group ($t = 2.51$, $P < .05$).

There were no differences in the heart rate between the life duration groups in these young rats (table 1).

In old age (table 2), the long lived group had significantly lower systolic blood pressures ($t = 2.49$, $P < .05$) and heart rates ($t = 3.48$, $P < .01$) than the very long lived group.

Systolic Blood Pressure, Heart Rate and Lung Disease.—Postmortem examination of the lungs showed the presence of lung abscesses in 80 per cent of the rats. When blood pressure and

* Standard error.

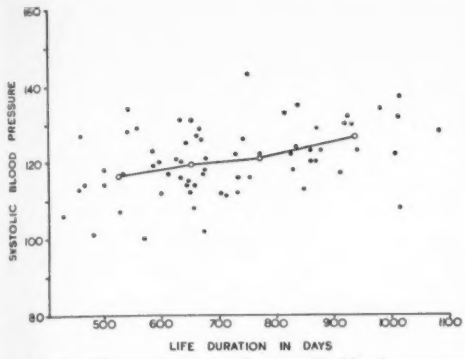

Fig. 1. The variation in the systolic blood pressure of 68 young male rats, with life duration. The mean blood pressures of each life duration group are joined by straight lines. Blood pressures were recorded at 340 ± 0.7 days.

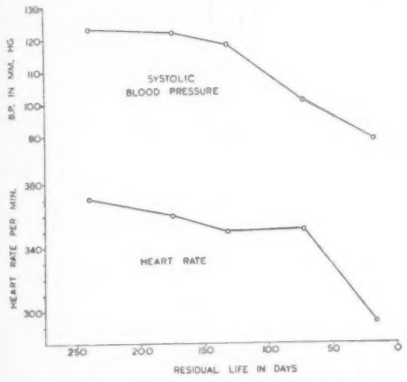

Fig. 2. The systolic blood pressure and heart rate of male rats grouped according to their residual life. The number of rats in each residual life group ranged from 11 to 13.

heart rate were related to lung pathology (table 3), rats with diseased lungs at autopsy had lower systolic blood pressures and heart rates than those with healthy lungs. Rats with lung disease at autopsy had significantly lower heart rates when young ($t = 2.26$, $P<.05$) and significantly lower systolic blood pressures when old ($t = 3.25$, $P<.01$). It is interesting to note that rats with healthy lungs showed little or no change in blood pressure between the ages of 340 and 675 days, whereas over the same period rats with diseased lungs had a significant fall in blood pressure (table 3). This difference was not found in the case of heart rates, which decreased with age in both diseased and healthy rats (table 3).

Pre-mortal Fall in Systolic Blood Pressure and Heart Rate.—A comparison of 2 life duration classes (long lived and very long lived) in youth (table 1) and in old age (table 2) revealed a fall in systolic blood pressure with age, which was more pronounced in the group with the shorter life duration. The fall in systolic pressure was much greater in the long lived group, which in old age had an average residual life (time between blood pressure determination and death) of 95 days, as against 264 days for the very long lived group. This observation led to the idea of a pre-mortal fall in systolic blood pressure. This concept was studied by grouping blood pressures into classes according to the

TABLE 1. SYSTOLIC BLOOD PRESSURE AND HEART RATE IN YOUNG MALE RATS OF AGE 340 ± 0.7 (S.E.) DAYS, IN RELATION TO LIFE DURATION.

Group	Life Duration in Days (Range)	Number	Systolic Blood Pressure (mm. Hg)	Heart Rate (per Min.)
Very Short Lived	526±13.1* (428–600)	17	116.6±2.4	378±10.6
Short Lived	655±5.4 (619–700)	17	119.1±2.0	374±7.7
Long Lived	770±12.1 (704–846)	17	121.4±2.1	381±13.3
Very Long Lived	939±16.2 (857–1084)	17	126.9±2.3	378±6.7
Whole Group	726±19.3 (428–1084)	68	121.0±2.2	378±4.8

* S.E. $= \sqrt{\frac{\Sigma d^2}{n\ (n-1)}}$

TABLE 2. SYSTOLIC BLOOD PRESSURE AND HEART RATE IN OLD MALE RATS OF AGE 675 ± 0.6 (S.E.) DAYS, IN RELATION TO LIFE DURATION.

Group	Life Duration in Days (Range)	Number	Systolic Blood Pressure (mm. Hg)	Heart Rate (per Min.)
Long Lived	770±12.1 (704–846)	17	104.8±6.4	330±13.6
Very Long Lived	939±16.2 (857–1084)	17	122.8±3.3	383±7.1
t	8.36		2.49	3.48
P	<.01		<.05	<.01

TABLE 3. LUNG DISEASE AT AUTOPSY IN RELATION TO SYSTOLIC BLOOD PRESSURE AND HEART RATE.

Lungs at Autopsy	Systolic Blood Pressure (mm. Hg)		Heart Rate (per Min.)	
	Youth	Old Age	Youth	Old Age
Healthy (N)	126.0 ±2.8 (13)	129.1 ±5.1 (10)	400.0 ±10.2 (13)	374.5 ±14.0 (12)
Diseased (N)	119.7 ±4.1 (50)	106.7 ±4.6 (25)	373.9 +5.4 (50)	357.8 ±9.4 (25)
t	1.25	3.25	2.26	1.00
P	>.05	<.01	<.05	>.05

TABLE 4. THE PRE-MORTAL FALL IN THE SYSTOLIC BLOOD PRESSURE AND HEART RATE OF MALE RATS.

Residual Life in Days (Range)	238.6 ±3.1 (221–249)	174.8 ±4.2 (153–200)	132.5 ±4.5 (105–149)	73.2 ±4.3 (55–96)	17.6 ±4.5 (3–43)
Number	12	13	11	11	11
Systolic Blood Pressure (mm. Hg)	122.5 ±4.1	122.3 ±3.4	118.5 ±3.2	101.2 +6.7	80.9 ±5.6
Heart Rate (per Min.)	370.5 ±9.6	360.1 ±10.0	350.4 ±7.6	351.0 ±9.1	293.6 ±14.7

residual life of the rat (table 4). A distinct fall in systolic blood pressure occurred in the last 100 days of life (fig. 2), which is equivalent to 10 years of human life. Significant reductions in systolic blood pressure were found in the 50-100 days ($t = 3.12$, $P<.01$) and the 1-50 days ($t = 5.78$, $P<.01$) residual life groups.

In a similar way a significant reduction in heart rate was detected during the last 50 days of life ($t = 3.31$, $P<.01$).

DISCUSSION

In this investigation only systolic blood pressure and heart rate were used as indices of cardiovascular function. Obviously in a study of cardiovascular aging, data on diastolic pressure and cardiac output would have been valuable, but the risk involved in the necessary arterial cannulation was not justified in a long term experiment.

Systolic Blood Pressure, Heart Rate, and Life Duration.—In man the incidence of hypertension rises sharply with age from about 10 per cent in young adults (under 40 years) to more than 50 per cent in old age (15, 25). A similar increase in the frequency of hypertension with age has been reported in the rat (3, 16). On the assumption that 140 mm. Hg is the upper limit of normal (3, 5) only 3 per cent of young and 12 per cent of old rats would be regarded as hypertensive in the present series. Because systolic hypertension was comparatively rare in this strain a much larger group of rats would be needed to study its effect on the mortality rate.

On the other hand, systolic hypotension was much more common in this strain and consequently was of greater importance in the forecast of life expectancy. Results from both young (table 1) and old rats (table 2) show that rats destined for a short life have low systolic blood pressure. At first glance this observation would seem contrary to human life insurance experience where hypotension is commonly associated with a reduced mortality (1, 6, 8, 11, 22, 25). It must be realized that the beneficial action of hypotension on life expectancy is only true in the absence of disease (6, 11, 25). In this study systolic hypotension was often found in sick rats, whose blood pressures were usually less than 110 mm.Hg and were occasionally as low as 50 mm.Hg.

Heart rate was of less importance in connection with life duration, since no differences were found between the mean heart rates of the 4 life duration groups in young rats (table 1). It was only in later life that heart rate was of prognostic value when lower heart rates were found among the shorter lived of the surviving rats (table 2).

Lung Disease and Cardiovascular Function. Because of the high incidence of pulmonary lesions at autopsy, lung disease must be regarded as one of the most important factors limiting the life expectancy of these rats. The pattern of disease in the rat is thus quite different from that found in man, where cardiovascular-renal diseases dominate the picture in old age (7, 17, 18, 24).

The effect of lung disease on cardiovascular function was studied by comparing the systolic blood pressures and heart rates of rats with and without lung disease at autopsy (table 3). In both youth and old age lower blood pressures and heart rates were found in animals with lung disease. In addition, only rats with diseased lungs at autopsy showed a decrease in

blood pressure with age (table 3). This was not so in the case of heart rate, which was decreased with age in both healthy and diseased rats, although diseased animals had lower heart rates at both ages (table 3). Earlier workers have reported a decrease in heart rate with age in man (14) and in the rat (2, 13).

Chronic lung disease in man is frequently associated with low systolic blood pressure (1, 9, 11, 21, 25). In these rats lung disease was probably the cause of both hypotension and the accompanying shortened life duration. If this were the case one would not expect hypotension to be associated with short life duration in young rats (table 1) which were still growing and seemed to be healthy. However, according to the work of Saxton (23), about 50 per cent of these rats at 340 days would have chronic lung disease. This clearly shows the need for tests which would detect lung disease at an early stage in the life cycle of the rat.

The relationship between systolic blood pressure and life expectancy in the rat differs from that found in man, probably because of the different pattern of disease responsible for death. Since infectious lung disease is rarely of importance in human longevity, only strains of rats which are resistant to pulmonary infection should be used in aging studies.

SUMMARY

Short lived rats had low systolic blood pressure in both youth and old age. Moderate falls in systolic blood pressure and heart rate occurred during the last 50 to 100 days of life. In youth and old age, rats with lung disease at autopsy had lower systolic blood pressures and heart rates than those with healthy lungs. The systolic blood pressure of rats with diseased lungs decreased with age, but no such change occurred in rats with healthy lungs. The heart rate decreased with age in rats both with and without lung disease at autopsy.

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THE SENESCENT LOSS OF BODY WEIGHT IN MALE RATS

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Involution is one of the most characteristic features of aging (5, 7, 9, 15, 18, 28). According to Roessle and Roulet (21) the over-all effect of atrophy in a number of organs is to produce a fall in body weight.

Various workers have reported a loss of weight in aging rats (2, 4, 7, 10, 11, 16, 23, 29), mice (8, 20, 26), and guinea pigs (22). While cachexia is a feature of the terminal stages in a number of diseases in man (1, 6, 12, 14, 24, 27, 30), there is also a gradual fall in body weight in normal old age (12, 14, 17, 24).

The purpose of the present study is to investigate the loss in weight of aging rats in relation to life duration, lung disease, food and water consumption, and feces and urine production.

MATERIALS AND METHODS

The senescent loss in body weight was studied in 68 male albino rats of a non-inbred Wistar strain, which were kept in a small air-conditioned room and fed a pelleted diet as described previously (11).

Animals were weighed once a week on a Chatillon compression balance from early adult life until natural death. From these data the maximum weight and the body weights at death, and at 50, 100, 150 and 200 days before death were obtained. The senescent loss in weight was calculated as the difference from the maximum weight.

The life duration of each rat was recorded and a gross examination of the lungs was made at autopsy. The effects of lung disease and tumors on the course of senescent loss in weight were studied in 30 rats with severe lung disease, in 30 rats with healthy lungs at autopsy (13 rats from the main group of 68, and 17 from other untreated groups), and in 3 rats with large abdominal or mammary tumors not included in the main series of 68 rats.

The senescent fall in body weight was studied in relation to the consumption of food and water and the production of feces and urine in 30 rats from the age of 528 days until death. At monthly intervals animals were placed individually in metabolism cages, and after a 2-day period of adaptation, each rat was supplied with 30 Gm. of crushed food pellets and 100 ml. of water. At the end of 24 hours, estimations of the remaining food and water were made, and the daily consumptions of food and water obtained by difference from the original values. The moist weight of feces collected over 24 hours was recorded. The daily production of urine was calculated by adding to the volume of urine collected an estimate of the urine remaining behind in the metabolism cage and funnel, as estimated from a determination of creatinine in the distilled water washings of these parts.

From these results the daily exchanges of food, water, feces, and urine in 20 rats were calculated at stages corresponding to weight losses of approximately 10, 50, 100, and 150 Gm. in 20 rats.

RESULTS

In the last 200 days of life the average body weight of 68 male rats decreased from 381.0 Gm. to 249.2 Gm. (table 1).

Body Weight Loss and Life Duration.—The mean loss in body weight from the maximum for each of the 4 life duration groups at 200, 150, 100, 50, and 0 days of residual life is given in table 2. Statistical analysis in table 3 revealed large differences between the residual life groups ($F = 160.5$, $P < .01$), indicating a real loss in weight as the animal approached death. The loss in weight depended on the life duration of the rat, as shown by a significant difference between life duration groups ($F = 12.1$, $P < .01$). The interaction of residual life with life duration was not significant ($F < 1$).

The effect of life duration on the senescent loss in weight was studied further by analysis of the variance between individual life duration groups (table 3). Most of the variation was found to stem from the significant difference between the very short lived and the short lived groups ($F = 18.1$, $P < .01$). Differences between the short lived and long lived groups, and between the long lived and very long lived

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groups were not significant. From figure 1 and table 2 it may be seen that during the last 100 days of life the rate of loss in weight was approximately the same for all 4 life duration groups, being about 100 Gm. in 100 days. Also figure 1 shows that, during the last 100 days of life, the loss in weight from the maximum in the very short lived group was about 30 Gm. less than that of the 3 longer lived groups. This difference was less marked at 200 and 150 days of residual life, when the loss in weight increased progressively with life duration.

Since the senescent loss in weight of the very short lived group was significantly less than that of the 3 longer lived groups, 2 regression equations were calculated for the prediction of life expectancy in future experiments. One equation was used for forecasts made before 600 days (the greatest life duration of the very short lived group), and the second equation for forecasts after 600 days. Since forecasts of life expectancy in rats losing weight before 600 days would involve mainly the very short lived and the short lived groups, data on these 2 groups were pooled, giving the equation $L = 403 - 184 \log_{10} \triangle W$, where L is the life expectancy in days, and $\triangle W$ is the loss in weight in Gm. from the maximum. For rats living longer than 600 days the combined results on the short, long, and very long lived groups yielded the equation $L = 613 - 282 \log_{10} \triangle W$.

Body Weight Loss in Relation to Lung Disease and Large Tumors.—Postmortem gross examination of the lungs showed the presence of lung abscesses in about 80 per cent of the animals. The extent of lung disease was judged

TABLE 1. THE CHANGE IN THE BODY WEIGHT OF 68 MALE RATS IN THE LAST 200 DAYS OF LIFE.

Residual Life (Days)	200	150	100	50	0
Body Weight (Gm.) ± S. E.	381.0 ±4.8	370.2 ±5.8	345.4 ±6.5	315.5 ±6.7	249.2 ±5.7

TABLE 2. THE SENESCENT LOSS OF BODY WEIGHT IN RELATION TO THE LIFE DURATION OF 68 MALE RATS.

Group	Life Duration (Range)	No.	Loss in Body Weight (Gm.) at Residual Life of: 200 Days	150 Days	100 Days	50 Days	0 Day (Death)
Very Short Lived	526±13.1* (428-600)	17	6.6	19.2	32.0	68.5	131.0
Short Lived	655±5.4 (619-700)	17	15.5	30.5	65.2	103.7	161.1
Long Lived	770±12.1 (704-846)	17	27.8	37.0	70.8	90.5	166.1
Very Long Lived	939±16.2 (857-1084)	17	36.3	51.6	67.5	93.0	156.8
Combined Short, Long and Very Long Lived Groups	788±17.6 (619-1084)	51	26.5 ±2.5*	39.7 ±4.2	67.8 ±5.1	95.8 ±5.5	161.3 ±6.1
Whole	726±19.3 (428-1084)	68	21.5 ±2.9	34.6 ±3.3	58.9 ±4.6	89.0 ±5.2	153.8 ±5.2

* S.E. $= \sqrt{\frac{\Sigma d^2}{n(n-1)}}$

TABLE 3. ANALYSIS OF VARIANCE OF THE SENESCENT LOSS IN BODY WEIGHT IN RELATION TO LIFE DURATION.

Source of Variation	Sum of Squares	df	Variance	F	P
Between Times	740,976	4	185,244	160.5	<.01
Between Life Duration Groups	42,018	3	14,006	12.1	<.01
Interaction (Groups × Times)	13,147	12	1,096	<1	>.05
Error	369,163	320	1,154		
Total	1,165,304	339			
Subgroup Analysis					
Between Very Short and Short Lived	20,923	1	20,923	18.1	<.01
Between Short and Long Lived	451	1	451	<1	>.05
Between Long and Very Long Lived	285	1	285	<1	>.05

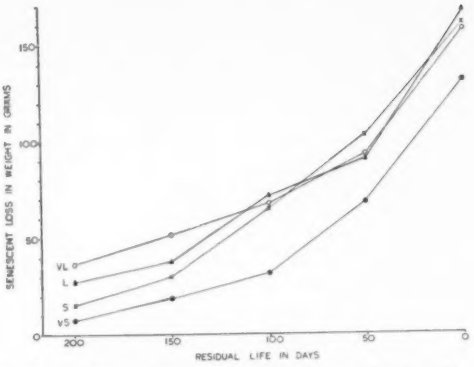

Fig. 1. The effect of life duration on the loss in weight from the maximum, during the last 200 days of life in 68 male rats. Rats are divided into 4 life duration groups: VS, very short lived; S, short lived; L, long lived; and VL, very long lived.

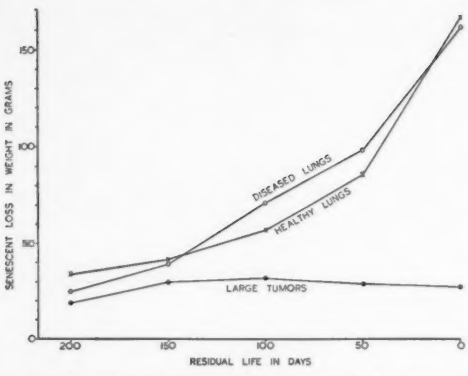

Fig. 2. The senescent loss of weight in 30 rats with healthy lungs and free of tumors, compared with the loss in 30 rats with diseased lungs and in 3 rats with large tumors.

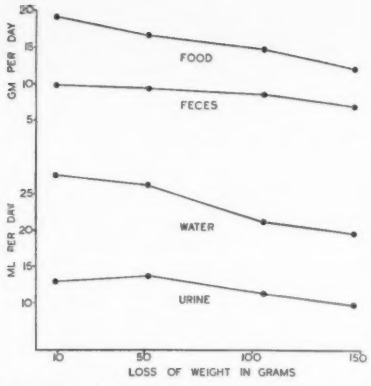

Fig. 3. The decline in consumption of food and water and the production of feces and urine, in relation to the senescent loss of weight in 20 male rats.

by estimating the area of the lung covered with abscesses. Animals with lesions involving more than 50 per cent of the external lung surface were said to have severe lung disease, while those with no macroscopic evidence of abnormality were said to have healthy lungs. The senescent loss of weight in 30 rats with severe lung disease was very similar to that in 30 rats with healthy lungs at autopsy (table 4 and fig. 2). Analysis of variance (table 5) showed a significant difference between times as expected ($F = 133.8$, $P < .01$), but the variation between diseased and healthy lungs was not significant ($F < 1$).

The development of large abdominal or mammary tumors diminished the apparent loss in weight before death (table 4 and fig. 2). These tumors are of rare occurrence in this strain, since only 3 cases were found in 175 post mortems. The weights of the tumors were 140, 140, and 160 Gm. respectively, which represented about 30 per cent of the total body weight. The loss in the mean tumor-free body weight of these 3 animals post mortem was approximately 160 Gm., which closely agreed

TABLE 4. THE SENESCENT LOSS IN BODY WEIGHT IN RELATION TO LUNG DISEASE AND LARGE TUMORS.

Post Mortem	Number	Residual Life in Days				
		200	150	100	50	0
Healthy Lungs...	30	32.2	40.2	56.6	85.5	165.8
Diseased Lungs...	30	24.8	39.5	71.8	98.8	160.8
Large Tumors....	3	10	30	32	29	28 (160)*

* Loss in tumor-free body weight at death.

TABLE 5. ANALYSIS OF VARIANCE OF THE SENESCENT LOSS IN BODY WEIGHT IN RELATION TO LUNG DISEASE.

Source of Variation	Sum of Squares	df	Variance	F	P
Between Times.....	694,616	4	173,654	133.8	<.01
Between Lung Groups.....	724	1	724	<1	>.05
Interaction (Lung Groups × Times).	6,560	5	1,312	1.01	>.05
Error.....	374,922	289	1,297		
Total.....	1,076,822	299			

TABLE 6. THE CONSUMPTION OF FOOD AND WATER AND THE PRODUCTION OF FECES AND URINE IN 20 MALE RATS AT 4 LEVELS OF SENESCENT LOSS IN WEIGHT.

Quantity Measured	Units	Value at Mean Weight Loss (Gm.) of:				F	P
		9.4 ±1.4	51.7 ±1.3	105.2 ±1.4	146.0 ±2.1		
Food Consumption	Gm./Day	19.0 ±0.51	16.7 ±0.53	14.7 ±0.44	12.0 ±0.87	22.6	<.01
Feces Production	Gm./Day	9.8 ±0.31	9.4 ±0.38	8.4 ±0.51	6.8 ±0.53	73.5	<.01
Water Consumption	Ml./Day	27.5 ± 3.2	26.1 ± 2.7	21.2 ± 2.7	19.6 ± 2.0	8.5	<.01
Urine Production	Ml./Day	12.8 ±0.61	13.6 ±0.57	11.3 ±0.76	9.8 ±0.62	8.3	<.01

with a mean of 153.8 Gm. for the 68 rats used in the main experiment.

Body Weight Loss in Relation to Exchanges of Solids and Fluids.—The consumption of food and water and the production of feces and urine by 20 rats at stages corresponding to the loss of 10, 50, 100, and 150 Gm. of body weight are given in table 6. These data show that the fall in body weight before death was accompanied by significant reductions in food consumption ($F = 22.6$, $P < .01$), feces production ($F = 73.5$, $P < .01$), water consumption ($F = 8.5$, $P < .01$), and urine production ($F = 8.3$, $P < .01$) (fig. 3).

DISCUSSION

With respect to body weight, the life cycle of the male rat consists of a stage of growth, characterized by a rapid increase in weight, followed by an equilibrium period of relatively constant weight, and terminated by the phase of senescence in which body weight falls as death approaches (10, 11).

Senescent Loss in Weight and Life Duration.—In the case of the very short lived group of rats, the curve showing the loss in weight from the maximum was displaced about 30 Gm. below the mean curve for the 3 longer lived groups (fig. 1). All 4 life duration groups would have followed a similar course of weight loss if the maximum weight of the very short lived group had been about 30 Gm. greater than observed. Since the very short lived group of rats reached its maximum weight at an average age of 364 days (11), at a time when the longer lived groups were still actively growing, growth was probably interrupted prematurely by disease or senescence leading to a low body weight maximum (11).

In the male rat, body weight seems to be influenced by two opposing forces, those of growth and senescence. When these two processes are in equilibrium, at about the time of attaining the maximum weight, there occurs a period of relatively constant weight. The length of this equilibrium period depends on the life duration of the rat, ranging from several days in very short lived animals to a few hundred days in very long lived animals. Consequently the very short lived rats pass rapidly into the senescent phase of weight loss, while the longer lived rats lose weight gradually over a longer period of time before passing into the senescent phase.

As a result of the gradual loss in weight over a long period of time, the long lived rats showed, at 200 and 150 days before death, proportionately greater losses in weight from the maximum than the short lived groups (table 2 and fig. 1). At a residual life of 200 days, the very long lived group had accumulated a loss in weight over a period of 257 days, as compared with 101 days for the long lived and 30 days for the short lived group. In the case of the very short lived group some rats were still gaining weight at a residual life of 200 days and therefore the average loss in weight of the group was small.

Once an animal passed into the terminal stage of life, which may be regarded as the last 100 days of life, the average rate of loss in weight was essentially the same in all 4 life duration groups (table 2 and fig. 1).

Senescent Loss in Weight and Disease.—In this local strain of the Wistar rat, lung disease is found in 80 per cent of males at autopsy. When the senescent loss in weight of rats with large areas of diseased lung observed at post mortem was compared with the loss in rats with healthy lungs, the curves were found to be almost identical (fig. 2). Therefore the loss in weight during the last 200 days of life was not altered by the presence of lung disease. This observation does not mean that lung disease has no effect on the life expectancy of the rat. In the main series of 68 rats, the 13 rats free of lung disease had a mean life duration of 861 ± 38 days, as against 691 ± 20 days for 50 animals with lung disease. Lung disease probably accelerates the onset of senescence, but once this stage is initiated the loss in weight is not influenced by this disease.

Very heavy tumors complicate the use of the senescent loss in weight as an index of aging. Large abdominal or mammary tumors reduce the apparent loss in weight. This effect is caused by the weight of the tumor, since the loss in the tumor-free body weight at death is approximately the same as that found in other animals. Probably the curve of the loss in tumor-free body weight would follow a similar course to that found in other animals.

Senescent Loss in Weight and the Exchanges of Solids and Fluids.—In man the loss of weight occurring in diseases like pulmonary tuberculosis, cancer, and Addison's disease is often attributed to starvation arising in various ways (6, 13, 24, 30). According to Keys (13), under-

nutrition may result from diminished food intake, increased food destruction, diminished absorption, diminished utilization and storage, increased excretion, or increased metabolism. However, the most frequent cause of undernutrition is thought to be the result of a diminished food intake (13, 30).

In the present study the intake of food and water and the output of feces and urine declined roughly in proportion to the fall in body weight. These results fail to indicate whether the loss in weight was due to a diminished food and water consumption or whether food and water intake became reduced because of the fall in body weight. Since body weight may be reduced experimentally by diminishing the intake of either food (3, 13, 14, 19) or water (25), it is likely that the observed drop in food and water consumption contributed to the loss in body weight.

SUMMARY

Aging male albino rats of the Wistar strain lost more than 30 per cent of their body weight during the last 200 days of life. The loss of weight from the maximum in the very short lived group of rats was significantly less than that in longer lived animals. The rate of loss in weight during the last 100 days of life was independent of life duration.

Even though lung disease reduced the life expectancy of the rat, it had no effect on the course of the senescent loss in weight. Large tumors reduced the apparent loss in weight, but when allowance was made for the weight of the tumor this discrepancy disappeared.

The senescent loss in body weight was accompanied by a decline in the consumption of food and water and in the production of feces and urine.

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HEXOSAMINE AND ACID-HYDROLYZABLE SULFATE CONCENTRATIONS OF CORONARY AND CEREBRAL ARTERIES IN INDIVIDUALS OF VARIOUS AGES*

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In a previous publication (1) from this laboratory the concentrations of hexosamine and acid-hydrolyzable sulfate of the aorta and pulmonary artery in individuals of various ages were reported. The present investigation was undertaken with the purpose of providing similar data for the human coronary and cerebral arteries.

MATERIAL AND METHODS

Sixty-one samples of the coronary and cerebral arteries were obtained fresh at autopsy at the St. Louis City Morgue.† The age of the individuals from whom the samples were derived ranged between 8 and 77 years.

The right and left coronary arteries were carefully removed from the myocardium by dissection; the cerebral blood vessels included the basilar artery, the circle of Willis, the anterior, middle, and posterior cerebral arteries, and their main branches. After separation of the adventitia, portions of the intima-media were employed for determination of hexosamine and acid-hydrolyzable sulfate. The analyses were carried out in duplicate as previously described (1). In addition, measurements of the dry weight and the cholesterol content (2) of the tissue were made on a portion of the arterial wall adjacent to that employed for hexosamine and sulfate analyses. Determinations of the total nitrogen content of the samples were carried out by Kjeldahl analysis when sufficient tissue was available.

RESULTS

Coronary artery samples.—The results of the determinations of hexosamine (N = 60) and acid-hydrolyzable sulfate (N = 60) on the individual coronary artery samples are presented in table 1, and the mean values observed for the various age groups are listed in table 2. The average hexosamine concentration found in the coronary artery tissue was 0.25 per cent (s.d. of distribution 0.066), calculated on the basis of wet tissue weight. If expressed on the basis of dry tissue weight, the mean hexosamine concentration of the samples was 0.97 per cent. As seen from table 2 no significant difference in the average tissue concentrations of hexosamine was found between subjects aged 8-49 years and 50-77 years.

With regard to the acid-hydrolyzable sulfate content of the coronary artery tissue the average concentration observed was 0.054 per cent (s.d. of distribution 0.024), calculated on the basis of wet tissue weight, and 0.212 per cent, expressed on the basis of dry tissue weight. As in the case of hexosamine no significant difference in the mean tissue concentrations of sulfate was found between 8-49 and 50-77 year-old subjects (table 2).

Cerebral artery samples.—The results of the determinations of hexosamine (N = 60) and acid-hydrolyzable sulfate (N = 60), carried out on the cerebral artery samples, have been included in tables 1 and 2. As seen from the tables, the mean concentrations of both these compounds were found to be lower in the cerebral arteries than in the coronary artery samples. Thus the average hexosamine concentration of the cerebral artery samples was only 0.18 per cent (s.d. of distribution 0.035), expressed on the basis of wet tissue weight, and 0.75 per cent, calculated on the basis of dry tissue weight. The corresponding sulfate values were 0.042 per cent (s.d. of distribution 0.015), and 0.175 per cent. In contrast to the coronary artery samples the average hexosamine and sulfate values of the cerebral artery tissue were found to be significantly higher for the samples derived from subjects aged 50-77 years than for samples obtained from younger individuals (table 2).

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TABLE 1. HEXOSAMINE AND ACID-HYDROLYZABLE SULFATE CONCENTRATIONS OF 61 HUMAN CORONARY AND CEREBRAL ARTERY SAMPLES.

			Coronary Arteries					Cerebral Arteries				
No.	Age (Years)	Sex, Race	Dry Matter, %	Nitrogen, % of Wet Weight	Cholesterol, % of Wet Weight	Hexosamine, % of Wet Weight	Acid-Hydrol. SO_4, % of Wet Weight	Dry Matter, %	Nitrogen, % of Wet Weight	Cholesterol, % of Wet Weight	Hexosamine, % of Wet Weight	Acid-Hydrol. SO_4, % of Wet Weight
1	8	FW	25.0		0.14	0.16	0.022	26.7	4.19	0.19	0.14	0.046
2	25	MC	23.4		0.35	0.50	0.084	26.6	4.10	0.18	0.18	0.045
3	25	FW	28.3			0.25	0.030	24.9	3.30	0.17	0.17	0.024
4	29	MW	21.8		0.35	0.20	0.058	24.2	3.49	0.14	0.17	0.034
Mean...			24.6		0.21	0.28	0.049	25.6	3.77	0.17	0.16	0.037
5	31	MW	25.0	2.62	0.47	0.24	0.086	25.0	3.40	0.35	0.11	0.058
6	33	MC	18.0		0.36	0.20	0.072	21.7		0.23	0.16	0.040
7	36	MW	22.0	2.82	0.24	0.21	0.058	37.4	4.78	0.35	0.15	0.084
8	36	MC	24.6		1.36	0.30	0.029	22.3	3.01	0.23	0.14	0.015
9	37	MC	27.6		0.55	0.25		25.2		0.45	0.21	
10	38	FC	22.0	2.83	0.30	0.28	0.064	25.4	4.08	0.18	0.14	0.030
11	38	FC	21.7	2.21	0.28	0.27	0.070	24.1		0.17	0.14	0.039
12	39	FC	28.9		0.84	0.22	0.043	25.9		0.15	0.19	0.025
Mean...			23.8	2.63	0.55	0.25	0.060	26.0	3.82	0.26	0.16	0.042
13	40	FC	24.1	3.18	0.90	0.29	0.041	26.4	3.76	0.32	0.23	0.031
14	41	MW	24.3	3.24	1.39	0.32	0.081	26.0	3.52	0.63	0.19	0.056
15	42	MC	22.1	2.81	0.49	0.27	0.022	22.2	2.83	0.27	0.18	0.015
16	43	MW	25.0		3.00	0.14	0.037	25.0		1.06	0.12	0.050
17	44	MW	22.9	2.56	1.04	0.14	0.025	18.4	2.52	0.40	0.19	0.013
18	46	MC	21.4	2.74	0.78	0.21	0.035	21.5	2.86	0.25	0.15	0.035
19	48	MC	23.6	2.34	1.22	0.25	0.041	21.7	3.01	0.35	0.16	0.010
20	49	MW	24.6		0.94	0.23	0.056	23.8	3.26	0.26	0.18	0.029
21	49	FW	22.2		0.88	0.24	0.041	22.3	2.79	0.24	0.13	0.035
22	49	FW	26.8	2.84	3.00	0.22	0.052	23.5	3.13	0.50	0.15	0.047
Mean...			23.7	2.83	1.36	0.23	0.043	23.1	3.08	0.43	0.17	0.032
23	50	MW	35.4	2.41	0.88	0.27	0.018	23.1	3.23	0.16	0.15	0.020
24	50	MC	29.0		0.68	0.19	0.088	23.1	2.21	0.31	0.15	0.048
25	50	FW	22.3		0.39	0.27	0.091	23.0		0.30	0.17	0.075
26	51	MW	32.1	3.13	1.38	0.30	0.040	22.9	3.05	0.21	0.14	0.046
27	51	MW	25.8	2.28	1.42	0.27	0.058	23.1	3.08	0.26	0.18	0.030
28	51	MC	23.2	2.98	0.76	0.27	0.060	22.8	3.02	0.29	0.21	0.033
29	52	MW	39.1	3.12	2.40	0.19	0.010	23.2	2.84	0.30	0.19	0.027
30	52	MW	25.5		1.02	0.25	0.104	23.1	3.05	0.30	0.17	0.059
31	53	MW	23.0	2.55	0.42	0.26	0.060	25.3		0.40	0.19	0.035
32	53	FC	22.4	3.40	1.05	0.27	0.076	24.8	3.00	2.29	0.22	0.047
33	53	FC	24.1	3.42	1.20	0.29	0.074	22.5		0.56	0.22	0.056
34	54	MW	21.1		0.23	0.13	0.044	22.9		0.45	0.16	0.054
35	54	MW	31.0	3.77	0.71	0.26	0.058	22.4	2.49	0.85	0.20	0.044
36	54	MW	36.8	3.12	2.75	0.30	0.072	23.3	2.97	0.60	0.15	0.044
37	54	MC	23.9	3.01	0.30	0.36	0.080	20.6	2.81	0.24	0.20	0.044
38	55	MW	27.1	2.81	1.38	0.21	0.055	23.3	2.69	0.51	0.21	0.044
39	55	MW	22.7	3.50	0.49	0.24	0.056	24.7	3.34	0.24	0.20	0.024
40	55	MW	25.3	2.78	1.50	0.19	0.079	23.5	3.06	0.46	0.14	0.067
41	57	MW	25.8	2.63	0.87	0.36	0.036	22.8	3.14	0.33	0.15	0.035
42	58	MC	33.0	3.22	2.96	0.38	0.092	23.0	2.77	1.34	0.24	0.049
43	58	MC	22.2	3.59	0.41	0.33	0.056	23.8	3.49	0.27	0.21	0.021
44	59	MC	25.0	2.62	1.21	0.15	0.017	23.8	2.76	0.60	0.21	0.049
45	59	FW	25.2	2.68	0.99	0.26	0.076	25.3	3.30	0.37	0.13	0.046
Mean...			27.0	3.01	1.10	0.26	0.061	23.4	2.96	0.51	0.18	0.043
46	61	FW	33.4	3.09	1.58	0.21	0.032	25.0	2.83	4.42	0.25	0.054
47	63	MW	23.0	2.58	1.32	0.23	0.077	22.2	2.88	0.46	0.15	0.059
48	65	MW	34.0	2.81	1.62	0.20	0.042	26.5	3.55	0.38	0.16	0.038
49	65	MW	25.0	2.23	0.38	0.19	0.019	22.6	3.02	0.49	0.15	0.046
50	65	MW	25.0	2.70	2.00	0.23	0.073	25.0	3.29	0.60	0.14	0.059
51	66	MW	27.3	2.85	0.76	0.32	0.104	24.9	3.55	0.70	0.24	0.049
52	67	MW	25.0	1.97	1.62	0.12	0.013	24.2	3.02	0.64	0.18	0.045
53	68	MW	26.8	2.52	0.98	0.23	0.065	22.4	3.13	0.30	0.17	0.044
54	69	MW	45.0	5.61	1.78	0.33	0.074	21.8	2.90	0.26	0.18	0.041
55	69	MW	35.8	4.20	0.66	0.24	0.021	23.2	2.64	0.82	0.21	0.036
56	69	MW	25.0	2.05	0.90		0.035	26.3	3.42	0.66		0.062
Mean...			29.2	2.96	1.24	0.23	0.051	24.1	3.11	0.88	0.18	0.053
57	73	FW	28.6	1.33	1.19	0.19	0.022	24.6	3.24	0.56	0.19	0.047
58	76	MW	24.6	2.46	1.46	0.25	0.069	22.0	3.03	0.33	0.16	0.054
59	76	MW	25.7	2.86	0.97	0.21	0.061	24.4	3.07	0.53	0.20	0.050
60	76	FW	36.5	3.22	1.32	0.21	0.021	22.6	2.51	0.95	0.21	0.032
61	77	FW	30.8	3.61	1.48	0.36	0.060	27.2	3.46	1.25	0.28	0.048
Mean...			29.3	2.73	1.28	0.24	0.047	24.2	3.06	0.73	0.21	0.046
Grand Mean...			26.4	2.90	1.05	0.25	0.054	24.0	3.15	0.53	0.18	0.042

TABLE 2. MEAN HEXOSAMINE AND ACID-HYDROLYZABLE SULFATE VALUES OF CORONARY AND CEREBRAL ARTERIES IN VARIOUS AGE GROUPS.

Age Group (Years)	N	Coronary Arteries				Cerebral Arteries			
		Hexosamine		Acid-Hydrol. SO_4		Hexosamine		Acid-Hydrol. SO_4	
		% of Wet Weight	% of Dry Weight	% of Wet Weight	% of Dry Weight	% of Wet Weight	% of Dry Weight	% of Wet Weight	% of Dry Weight
8 – 29	4	0.28	1.14	0.049	0.202	0.16	0.65	0.037	0.145
30 – 39	8	0.25	1.05	0.060	0.269	0.16	0.62	0.042	0.156
40 – 49	10	0.23	0.98	0.043	0.180	0.17	0.74	0.032	0.136
50 – 59	23	0.26	0.99	0.061	0.238	0.18	0.78	0.043	0.186
60 – 69	11	0.23	0.78	0.051	0.196	0.18	0.77	0.053	0.222
70 – 77	5	0.24	0.86	0.047	0.172	0.21	0.85	0.046	0.192
Mean		0.25	0.97	0.054	0.212	0.18	0.75	0.042	0.175
s. d. of distribution		0.066	0.29	0.024	0.103	0.035	0.16	0.015	0.058
8 – 49	22	0.245	1.03	0.050	0.214	0.163	0.68	0.036	0.144
50 – 77	39	0.250	0.92	0.056	0.212	0.185	0.79	0.045	0.192
t of difference		0.26	1.34	0.98	0.08	2.66	2.86	2.14	3.32

DISCUSSION

The mean hexosamine concentrations of the coronary and cerebral arteries found in the present study are, respectively, 83 and 60 per cent of the average concentration found in the aorta, and the acid-hydrolyzable sulfate values 72 and 56 per cent of the aortic sulfate concentration (1). The lower sulfate values observed in the coronary and cerebral blood vessels would indicate a lower content of sulfate-containing acid mucopolysaccharides in these arteries. A comparison of the hexosamine concentrations with the acid-hydrolyzable sulfate values of the coronary and cerebral artery samples shows a hexosamine content of the tissue in excess of that which can be accounted for on the basis of the values for acid-hydrolyzable sulfate, suggesting the presence of notable quantities of non-chrondroitin sulfate hexosamine in the arterial wall. Thus a calculation (1) of the non-chrondroitin sulfate hexosamine content of the coronary artery samples showed a mean value of 0.150 per cent, expressed on the basis of wet tissue weight; for the cerebral artery samples the average value found was 0.102 per cent. These concentrations are, respectively, 60 and 57 per cent of the total hexosamine values found.

SUMMARY

Determinations were made of the concentrations of hexosamine and acid-hydrolyzable sulfate on 61 samples of the coronary and cerebral arteries obtained from individuals aged 8-77 years. The average concentrations of hexosamine and acid-hydrolyzable sulfate found in the wet tissue of the coronary arteries were, respectively, 0.25 and 0.054 per cent. The corresponding values for the cerebral arteries were distinctly lower, the average hexosamine concentration being 0.18 per cent, and the mean sulfate content 0.042 per cent.

No significant differences in the hexosamine and sulfate concentrations were found between coronary artery samples derived from subjects aged 8-49 years and 50-77 years. In contrast to this, both the hexosamine and sulfate concentrations of the cerebral arteries from the 50-77-year age group were significantly higher than the values observed for the 8-49 year old individuals.

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THE URINARY EXCRETION OF DEHYDROEPIANDROSTERONE AND TOTAL 17-KETOSTEROIDS IN AGED MEN AND WOMEN

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Determination of the urinary levels of dehydroepiandrosterone (DHA) provides a fair index of adrenocortical activity (10). The quantity of DHA excreted in the urine of healthy young men and women has been estimated (2); however, values for aged subjects have not been reported, although plasma concentration of DHA has been shown recently (11) to decrease with advancing age. In the present investigation, urinary levels of DHA and also 17-ketosteroids (17-KS) were measured in aged men and women and in young men. These levels were found markedly decreased in aged subjects. The ratio of DHA to 17-KS also fell in the aged subjects.

METHODS

Subjects

Collection of Urine. — Subjects, who were ambulatory, well, and cooperative, were chosen from among the residents of The Home for the Jewish Aged in Philadelphia. Twenty-four hour urine collections for 17-KS and DHA analyses were obtained, under supervision, from 12 men (64-90 years) and 20 women (64-91 years). Eight young men (20-35 years) served as a control group; the results obtained by Bray and Merivale (2) on the DHA and total 17-KS urinary levels of young adult men and women were compared and found to be in substantial agreement. All urine specimens were collected under toluol, and immediately worked up; in some cases, the urine was stored for short periods at −20 C. Short term storage under such conditions was found to have no discernable effect upon the analytic results.

Urine Hydrolysis Procedures

A. *Buffered Hydrolysis at pH 4.7.*—The volume of the 24-hour urine collection was measured; an aliquot of 400 cc. was taken and the pH adjusted to about 4.7 with acetic acid. The aliquot was hydrolysed by a modification of the method of Bitman and Cohen (1) by adding 40 cc. of 2.5 M sodium acetate buffer at pH 4.7 and refluxing for 4 hours. The cooled hydrolysate was extracted with ether (4 x 50 cc.). The extracted or "spent" urine was retained for further processing as described below. The ether extract was washed with 4 per cent NaOH (4 x 25 cc.), then repeatedly with water until neutral and the extract was evaporated to dryness on a steam bath.

B. Acid Hydrolysis.—The spent urine retained from the preceding process was brought to a boil, 15 per cent by volume of concentrated HCl was then added and refluxing continued for exactly 10 minutes. The hydrolysate was cooled under tap water and extracted with ether (4 x 25 cc.); the ether extract was washed with 4 per cent NaOH (4 x 25 cc.), then with water until neutral, and the extract was evaporated to dryness.

DHA and Total 17-KS Determination

The neutral ether residues from procedures A and B above were treated separately with Girard's reagent T by the method of Pincus and Pearlman (8) in order to obtain the respective ketonic fractions. Determination of the 17-KS content of the ketonic fractions was made by a modified Holtorff-Koch procedure as described by Munson and Kenny (5). Determination of the DHA content of the ketonic fraction from procedure A was made by the Pettenkofer color reaction according to the procedure described by Munson and associates (4). This fraction contains practically all the urinary DHA as shown by Bitman and Cohen (1) and confirmed in the present study by Pettenkofer determination of the ketonic fraction of procedure B.

RESULTS

The individual values for the urinary DHA and 17-KS levels and the percentage of 17-KS excreted as DHA of the subjects studied are

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listed in table 1. These data form the basis for table 2, which shows the mean value for the items studied according to age and sex. The daily urinary 17-KS excretion values for old people are much lower than those in young people, in accord with the findings of other investigators (3, 9). The DHA values have fallen from 3.4 ± 1.8 mg./24 hr. in young adult men to 0.5± 0.3 mg./24 hr. in aged men; and from 4.0 ± 1.5 mg./24 hr. in the adult young women (data of Bray and Merivale, 2) to 0.4 ± 0.1 mg./24 hr. in the old women. An alteration in the pattern of urinary excretion of total 17-KS and DHA is indicated by a comparison of the percentage of 17-KS excreted as DHA in the young and aged groups. While the levels of both 17-KS and DHA decline with age, the percentage of 17-KS excreted as DHA fell from 34.1 ± 19.0 in the young men to 12.1 ± 5.1 in the aged men. A decrease of similar magnitude is observed if the values for the women in Bray and Merivale's study (2) are compared with the values of the aged women in the present study.

TABLE 1. URINARY 17-KETOSTEROID AND DEHYDROEPIANDROSTERONE LEVELS IN OLD AND YOUNG MEN AND OLD WOMEN.

Men					Women				
Subject No.	Age	Mg. 17-KS/ 24 hr.	Mg. DHA/ 24 hr.	% 17-KS as DHA	Subject No.	Age	Mg. 17-KS/ 24 hr.	Mg. DHA/ 24 hr.	% 17-KS as DHA
28	20	7.53	10.20	72.4	94	64	5.08	0.33	6.45
50	24	10.20	4.18	41.0	34	70	0.96	0.09	8.83
51	24	13.62	4.72	34.7	86	70	5.38	0.91	16.86
55	26	17.75	5.07	28.6	90	7·	4.47	0.73	16.21
47	26	4.97	2.01	40.4	40	73	0.41	0.06	14.70
48	27	5.26	0.71	13.5	22	75	1.24	0.16	13.08
77	28	12.55	3.86	30.8	97	75	5.36	0.56	10.47
58	35	13.17	1.53	11.6	7	76	3.36	0.41	12.20
25	64	1.72	0.39	22.8	95	77	3.80	0.32	8.40
23	73	2.12	0.28	13.1	36	77	0.42	0.03	7.69
93	74	4.56	0.57	12.5	85	77	5.17	0.87	16.76
78	75	4.85	0.57	11.8	87	78	1.77	0.26	14.53
89	78	7.73	1.08	13.9	96	78	2.92	0.25	8.69
83	82	7.19	0.57	7.9	39	79	1.15	0.28	23.95
9	82	4.02	0.32	8.0	13	80	2.53	0.31	12.16
21	84	2.05	0.13	6.2	42	81	1.00	0.13	12.91
20	85	1.91	0.22	11.4	43	83	1.07	0.08	7.39
10	86	4.15	0.79	19.0	8	85	3.81	0.34	8.86
26	90	1.06	0.07	6.3	80	85	2.52	0.56	22.36
84	90	6.78	0.79	11.7	41	91	1.16	0.32	27.41

TABLE 2. THE MEAN URINARY 17-KETOSTEROID AND DEHYDROEPIANDROSTERONE LEVELS IN OLD AND YOUNG SUBJECTS.

Sex and Age	Number of Cases	Mg. 17-KS/ 24 hr. M±s. d.	Mg. DHA/ 24 hr. M±s. d.	% 17-KS excreted as DHA M±s. d.
Women (64–91 yr.)	20	2.7±1.9	0.4±0.1	13.5±6.3
Men (64–90 yr.)	12	4.0±2.3	0.5±0.3	12.1±5.1
Men (20–35 yr.)	8	10.6±4.5	3.4±1.8	34.1±19.0
Women (18-40 yr.)*	19	11.0±3.5	4.0±1.5	36.3±8.4
Men (19–34 yr.)*	21	13.3±4.9	4.4±2.4	32.8±8.8

* Data from Bray, and Merivale (2)

The mean values and the standard deviation of the distribution for the aged men and women and the young adult male controls are listed. Also included are the data published by Bray and Merivale (2) on the urinary steroid levels in young adults. The percentage of 17-ketosteroid excreted as DHA is also shown for each age group. M = Mean value; s.d. = standard deviation.

DISCUSSION

The data presented on the 17-KS and DHA urinary excretion levels for young adult men agree closely with those of Bray and Merivale (2).

If urinary DHA levels are to be regarded as a reliable reflection of adrenocortical activity, then it appears from our data (table 1) that such activity is considerably diminished in the aged. However, it has been observed (6) that urinary corticoid levels are not diminished appreciably with age nor are the plasma 17-hydroxycorticoids (11). The significance of the very low levels of urinary DHA in the aged will perhaps be better appreciated when the metabolic origin of DHA is more clearly understood than it is at present.

Recent investigations (9) in aged subjects suggest that the urinary level of certain 11-desoxy-17-ketosteroids declines more markedly than that of the corticoids; the level of those 17-ketosteroids which are metabolites of corticosteroids, namely the 11-oxy-17-ketosteroids, declines less with age than those which are metabolites of 11-desoxy-17-ketosteroids (6). The 11-desoxy-17-ketosteroids include such androgens as testosterone, Δ^4—androstenedione and dehydroepiandrosterone (7). In the present study, the decline in urinary levels of DHA with advancing age is greater than that of the total 17-ketosteroids. Since androgens are regarded as anabolic hormones because they promote nitrogen retention, the concomitant decrease in the anabolic gonadal hormones in aged subjects (9) and in anabolic-acting hormones of the adrenal could conceivably result in an excess of antianabolic or catabolic hormones and thus, perhaps promote the aging process.

SUMMARY

Urinary levels of dehydroepiandrosterone and total 17-ketosteroids were determined in

young and aged subjects. Values for both levels were found to fall with age. Dehydroepiandrosterone values fell from 3.4 ± 1.8 mg./24 hr. in young adult men (20-35 years) to 0.5 ± 0.3 mg./24 hr. in aged men (64-90 years); and from 4.0 ± 1.5 mg./24 hr. in the adult young women (18-40 years) (data of Bray and Merivale), to 0.4 ± 0.1 mg./24 hr. in the old women (64-91 years). This study has indicated that the percentage of 17-ketosteroids excreted as dehydroepiandrosterone declines with age in both men and women. It has been suggested that the fall in anabolic hormones in both the adrenal gland and the gonads is more rapid than the decline of catabolic hormones of adrenal origin.

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A COMPARISON OF URINARY STEROID EXCRETION PATTERNS IN YOUNG AND ELDERLY SUBJECTS BEFORE AND AFTER ACTH ADMINISTRATION

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In previous papers (7, 8) a method for analysis of urinary steroids in extracts of glucuronidase hydrolyzed two-day collections of urine and the steroid patterns obtained therefrom were described for a series of young normal and a few elderly subjects. This series has been enlarged to include patterns from 23 young (ages 20 to 40) and 14 elderly individuals (ages 60 to 91) of both sexes before and after administration of 50 I.U. of adrenocorticotrophic hormone (ACTH) per day.

METHODS

In brief, the procedure consisted of hydrolysis of 2 24-hour urine samples from each individual for both a control and an ACTH administration period with beef spleen glucuronidase followed by chromatography of the 48-hour methylene chloride extracts on silica gel (8). Three fractions of increasing polarity were obtained. These were further separated by paper chromatography into some 30 to 35 substances giving typical steroid color reactions. Where possible the metabolites were further characterized after elution from paper chromatograms by determination of ultraviolet absorption and sulfuric acid chromogen spectra.

RESULTS

Since further characterization of some of the previously demonstrated urinary metabolites (7, 8) has been made, a revised list of the regularly occurring color reacting substances grouped in relation to the mobility rates of known steroid compounds, along with their adsorption maxima in methanol in the ultraviolet and in sulfuric acid, are presented in tables 1 and 2. Those metabolites which have been isolated, crystallized, and in some cases identified after elution and pooling from paper chromatograms of the urinary extracts are indicated.

Tables 3 and 4 indicate the frequency of occurrence (in %) of the various color reacting metabolites present in urinary extracts of young and elderly individuals of both sexes before and following administration of ACTH.

The young men and young women have essentially the same mean frequency of occurrence of the less polar metabolites in control samples (85% versus 85%). After ACTH administration the frequency for samples from the young men dropped insignificantly to 80 per cent and rose insignificantly to 87 per cent for the female subjects. The male and female older subjects have similar metabolic patterns and frequencies (77% versus 77%) of detectable metabolites in the control samples. These frequencies are less than the 85 per cent found for the young individuals. The reduction is due largely to the absence of less polar metabolites No. 3 through No. 9, and seems to be augmented by ACTH administration to 67 per cent and 68 per cent, respectively.

In the case of the more polar and more characteristic corticosteroid metabolites there is no difference, essentially, in the frequency of occurence for male and female and young and elderly subjects before and after receiving ACTH. Cortisone, cortisol, tetrahydrocortisone (pregnanetroil-3α, 17α, 21-dione-11 20), and tetrahydrocortisol (pregnanetetrol-3α, 11β, 17α, 21-one-20) were detected in every extract. A number of other metabolites, No. 17, 19, 30, 32, 34, and 35, are present with almost as great frequency. Pregnanetriol-3α, 17α, 20α was found in the urine extracts of approximately half of the young men and women and with less frequency in the elderly subjects. Since this metabolite was not visualized by color reactions but was located either by its proximity to metabolite No. 22 or by its mobility rate and identified by its sulfuric acid chromagen spectrum, it may not have been detected in every case.

In more recent determinations of steroid patterns in a series of young and elderly subjects two additional metabolites, not included in tables 1 and 2, have been noted to occur with regularity. These are detected by means of a test for steroids with C-21 glycerol side chains

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TABLE 1. LESS POLAR URINARY METABOLITES IN ORDER OF DECREASING RUNNING RATES.

Standard Compounds	Urinary Metabolites	Maxima in MeOH mμ.	Maxima in H_2SO_4 mμ.
Androsterone	1. 17-KS-Androsterone?		Max. 510 Zim. *
Etiocholanol-3α-one-17	2. Etiocholanol-3α-one-17†		Max. 510 Zim. *
	3. C-21-CH_3? or C_{11}		
Δ^4-Androstenedione-3,17	4. C-21-CH_3? or C_{12}		
	5. α-ketol, unsaturated		
Allopregnanol-21-dione-3, 20			
Desoxycorticosterone	6. α-ketol? α, β-unsaturated ketone	230-240	285, 365-375
21-Hydroxypregnenolone	7. α-ketol		
Δ^4-Pregnenol-17α-trione-3, 11, 20	8. α-ketol?		
	9. α-ketol?		
11-Dehydrocorticosterone			
	10. α ketol		
Corticosterone			
	11. 17-KS? non-adrenal origin?‡	247	255, (390-405) §
	12. α-ketol		
	13. α, β-unsaturated ketone	?	275, 345
	14. α-ketol		
Pregnanediol-17α, 21-trione-3, 11, 20	15. Unsaturated ketone ‖	242, 260, 295	265, 330, (415-430)
Pregnanetriol-11β, 17α, 21-dione-3, 20	16. α-ketol		340, 400-405, (505-510)

* Maximum in Zimmermann reagent.
† Metabolite has been isolated, crystallized, and identified by infrared analysis.
‡ Metabolite has been isolated, crystallized, but unidentified.
§ ( ) Indicates plateau rather than maximum.
‖ This unidentified metabolite is identical to compound No. 8, isolated from human and bovine placenta by Pearlman (3).

TABLE 2. MORE AND MOST POLAR URINARY METABOLITES IN ORDER OF DECREASING RUNNING RATES.

Standard Compounds	Urinary Metabolites	Maxima in MeOH mμ.	Maxima in H_2SO_4 mμ
	More Polar		
	17. Δ^4-androstenol-11β-dione-3, 17 *	238	285, 375
	18. α-ketol		
Corticosterone	19. α-ketol, α- β, unsaturated ketone	240	280-285, 335-340, 365-390, 445-450
	20. α-ketol		295
Pregnanediol-17α, 21-trione- 3, 11, 20	21. α-ketol		265, 315-335, 415 (495-500)
	22. α-ketol? and pregnanetriol-3α, 17α, 20α*		330 300, 435, 500
Pregnanetriol-11α, 17α, 21-dione-3, 20	23. α-ketol		310-330, 420
Cortisone	24. Cortisone	238	285, 345, 415
	25. α, β-unsaturated, -non-adrenal origin †	235-238	285, 343, 440
Cortisol	26. Cortisol	240	285, 395, 475
	27. (see 34)		
Tetrahydrocortisone	28. Tetrahydrocortisone *		330, 415
Tetrahydrocortisol	29. Tetrahydrocortisol *		330, 415, 510
	30. α-ketol		260-265, 310-315, (390-400)
	31. α-ketol		260,275, 330-335, 385-395
	Most Polar		
Corticosterone	32. α-ketol		260,310-320
Pregnanediol-17α, 21-trione-3, 11, 20	33. α-ketol		280-290 (385-400)
	34. (27) α-ketol		265-270, 305, 425
Tetrahydrocortisone	35. α, β-unsaturated Ketone ‡	238-240	240, 280-290, (390-400)

* Metabolite has been isolated, crystallized, and identified by infrared analysis.
† Appears to be similar to compound X-6, described by Gray and associates (1).
‡ Metabolite has been isolated, crystallized, but unidentified.

TABLE 3. THE FREQUENCY (IN %) OF THE OCCURRENCE IN GLUCURONIDASE—HYDROLYZED URINES BEFORE AND AFTER ACTH ADMINISTRATION OF METABOLITES HAVING STEROID COLOR REACTIONS.

Less Polar Silica Gel Eluates

Subjects	Young Men		Young Women		Older Men		Older Women	
Number of Subjects	11		12		7		7	
Median Age	31		23		70		80	
Comp. No.. Description	Before ACTH	After ACTH	Before ACTH	After ACTH	Before ACTH	After ACTH	Before ACTH	After ACTH
1. 17 KS-androsterone?	91	100	75	83	57	50	43	43
2. Etiocholanol-3α-one-17	100	100	92	100	78	86	85	100
3. 21-CH_2? or C_{19}	82	73	92	83	64	57	85	43
4. 21-CH_2? or C_{19}	100	100	75	67	64	57	43	43
5. α-Ketol, unsaturated	82	55	75	83	64	50	85	57
6. α-Ketol?, α, β unsaturated	100	82	92	100	93	78	85	57
7. α-Ketol?	55	36	92	92	64	50	57	57
8. α-Ketol?	82	82	83	83	86	43	85	29
9. α-Ketol?	100	91	100	100	100	71	100	43
10. α-Ketol	73	82	75	83	86	71	100	100
11. 17-KS? non-adrenal origin	100	100	100	100	100	100	100	100
12. α-Ketol	73	91	83	92	71	78	71	100
13. α, β unsaturated Ketone	36	45	50	58	43	21	57	14
14. α-Ketol	100	64	83	67	86	86	85	100
15. Unsaturated Ketone	100	91	92	100	100	100	100	100
16. α-Ketol	82	91	100	100	71	86	43	71
Average Frequency	84.8	80.2	84.9	86.9	76.7	67.8	76.5	66.1

TABLE 4. THE FREQUENCY (IN %) OF THE OCCURRENCE IN GLUCURONIDASE—HYDROLYZED URINES BEFORE AND AFTER ACTH ADMINISTRATION OF METABOLITES HAVING STEROID COLOR REACTIONS.

More and Most Polar Silica Gel Eluates

Subjects	Young Men		Young Women		Older Men		Older Women	
Number of Subjects	11		12		7		7	
Median Age	31		23		70		80	
Comp. No., Description	Before ACTH	After ACTH	Before ACTH	After ACTH	Before ACTH	After ACTH	Before ACTH	After ACTH
17. Δ⁴-androstenol-11β-dione-3, 17	91	91	92	92	93	86	85	85
18. α-Ketol	64	73	100	92	57	71	71	57
19. α-Ketol-a, β unsaturated Ketone	100	100	100	100	93	100	100	100
20. α-Ketol	73	73	75	75	57	78	29	43
21. α-Ketol	100	100	83	83	93	86	85	85
22. α-Ketol? + Pregnanetriol-3α, 17α, 20α	73(45)*	64(45)*	92(55)*	83(55)*	78(57)*	71(43)*	71(29)*	71(29)*
23. α-Ketol	55	64	58	58	43	29	43	43
24. Cortisone	100	100	100	100	100	100	100	100
25. α, β unsaturated, non-adrenal origin	91	91	100	100	100	93	100	85
26. Cortisol	100	100	100	100	100	100	100	100
28. Tetrahydrocortisone	100	100	100	100	100	100	100	100
29. Tetrahydrocortisol	100	100	100	100	100	100	100	100
30. α-Ketol	100	100	92	100	100	86	100	100
31. α-Ketol	45	45	75	58	78	78	57	100
32. α-Ketol	100	100	100	100	86	100	100	100
33. α-Ketol	83	73	83	75	57	93	71	100
34. (27) α-Ketol	100	100	100	100	100	100	100	100
35. α, β unsaturated Ketone	91	100	75	92	100	100	100	100
Average Frequency	87.0	87.4	90.3	89.3	85.3	87.3	84.0	87.2
Average Frequency for all Metabolites	85.9	84.0	87.8	88.2	81.2	78.1	80.5	77.2

( )* — Pregnanetriol-3α, 17α, 20α.

(6) in which, after periodic acid oxidation, the products give Zimmermann reactions typical of a 17-ketosteroid. The two metabolites are more polar than tetrahydrocortisol. In the chloroform-formamide system one has a mobility on paper approximately 75 per cent of that for tetrahydrocortisol while the second has a mobility approximately half of that for tetrahydrocortisol. The former metabolite has no maximum in methanol in the ultraviolet. It has sulfuric acid maxima of 280, 410-415, which are similar to those for cortolone (pregnanetetrol-3α, 17α, 20α, 21-one-11) or an isomer thereof. Cortolone and its 20β isomer have been previously isolated from urine extracts by Fukushima and associates (2).

DISCUSSION

The patterns of color reacting urinary metabolites were quite reproducible from individual to individual. Occasionally, however, quantitative differences in amounts of certain metabolites excreted by one individual as compared to another were observed in the control chromatograms. In the case of each individual, ACTH administration produced obvious quantitative increases but did not seem to effect any obvious qualitative changes. Quantitative increases were particularly noted in the amounts of tetrahydrocortisone and tetrahydrocortisol excreted. The relative increases were as marked in the elderly as in the young subjects.

A comparison of the patterns for more and most polar urinary metabolites and the more typical corticosteroids, indicates that age, sex, and administration of 50 I.U. of ACTH effect no qualitative changes in the excretion of these metabolites.

Only in the case of the less polar metabolites is there any indication of changes with increasing age wherein the incidence of occurrence of detectable metabolites, particularly No. 3 through 9, is reduced somewhat as compared to that for young subjects. ACTH administration seems to enhance, in some elderly subjects, the disappearance of these detectable metabolites. These observed qualitative and quantitative decreases are conceivably a reflection of a previously demonstrated quantitative decline in urinary excretion of C-19 steroids with increasing age (4, 5).

SUMMARY

Excretion patterns of some 30 to 35 metabolites present in glucuronidase-hydrolyzed urine extracts and having steroid color reactions on paper chromatograms were determined for 11 young men, 12 young women, 7 elderly men, and 7 elderly women. Neither age, sex, nor administration of 50 I. U. of ACTH effected any significant qualitative change in the occurrence of the more characteristic corticosteroids (the more and most polar metabolites). Among these tetrahydrocortisone, tetrahydrocortisol, cortisone, and cortisol were detected in every extract.

A 10 per cent diminution before and a 20 per cent diminution after ACTH administration in the number of detectable less polar metabolites, which include 17-ketosteroids, was observed for the elderly subjects as compared with the young subjects.

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NEUROGENIC APPENDICOPATHY

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Neurogenic appendicopathy in old people presents a picture which in its symptoms is particularly difficult and sometimes impossible to distinguish clinically from acute or chronic appendicitis. Neurogenic appendicopathy is known in medical literature under the designation of "neurogenic appendicitis," in spite of the fact that it is not an inflammation of the appendix but rather a proliferation of the sympathetic nerve plexus. Neurogenic appendicopathy may occur after appendicitis or even be associated with it, but in most cases it constitutes its own clinical picture (3).

Neurogenic appendicopathy was first described in 1921, almost simultaneously by Maresch (7) in Vienna and Masson (8) in France. In its histologic manifestation the original lumen of the appendix is replaced by a proliferation of the sympathetic nerve plexus, which may give rise to neuroma-like growths (fig. 1). This proliferation of the terminal reticulum starts in the plexus mucosus, but it may also affect the plexus submucosus and myentericus. There is a conspicuous increase in eosinophilic leucocytes and argentaffin cells. The nervous tissue proliferates at the expense of the other tissues, with the lymphatic tissue being the most resistant to this process and consequently persisting the longest in the form of islands of various sizes. The pathologic changes in the nerve plexus may also spread to the blood vessels (9). With some practice these changes can be discerned in the standard hematoxylin-eosin slide. Special stains bring out these processes into clearer relief, particularly the method given by Coronini and Lassmann (2), which has a number of advantages over other special stains.

It is not only the microscopic picture which shows characteristic changes; the macroscopic texture of the appendix also furnishes certain clues as to the presence or absence of neurogenic appendicopathy. The appendix, in its consistency, has a coarser feel than normal. In most cases it is conspicuously ivory-colored, the serosa has an unusual luster (in as far as there are no adhesions); only a few blood-vessels are visible, and these seem to be thickened and stand out in plastic relief.

It can safely be assumed that the appearance of the vessels, since there are no arteriosclerotic changes, is due to a thickening of the walls, as described by the Swiss pathologist, Reubi, (9) under the name of "angioneuromatosis," and can be considered as the result of proliferation of the nervous elements as well as the blood vessels themselves (fig. 2).

The clinical manifestations of this disease are similar or equal to those of acute or chronic appendicitis. Frequently patients suffering from a neurogenic appendicopathy are found to be affected with a Porges-enteritis, a cholecystopathy, or a carcinomatous disease. A combination with allergic disorders has also been repeatedly observed. The polymorphism of the clinical picture of neurogenic appendicopathy is easily explained if we bear in mind the endocrine function of the argentaffin cells of Feyrter's "yellow-cell-organ" (4, 5), and consequently understand neurogenic appendicopathy as the morphologic expression of a disturbed correlation between the adeno-intestine and the neuro-intestine.

The therapy recommended for neurogenic appendicopathy, particularly by Knoflach (6), is appendectomy. With older patients it is necessary to be more cautious in advocating this measure. For those cases where the organic changes are confined to the appendix proper and the concomitant phenomena constitute reflex symptoms from other organs, appendectomy seems to be the preferable method, even in old age. In those cases, however, where neurogenic appendicopathy is only part of a general neurodystrophy, appendectomy may lead to a deterioration in the patient's general condition, which may pass into a rapidly progressing cachexia culminating after a short time in death. In such cases conservative treatment is preferred, in the form of dieting, psychotherapy, remedies to influence the neurovegetative system, and X-ray therapy (3).

It is stated (6) that neurogenic appendicopathy occurs most frequently between the 40th and 50th year of life and that it is extremely

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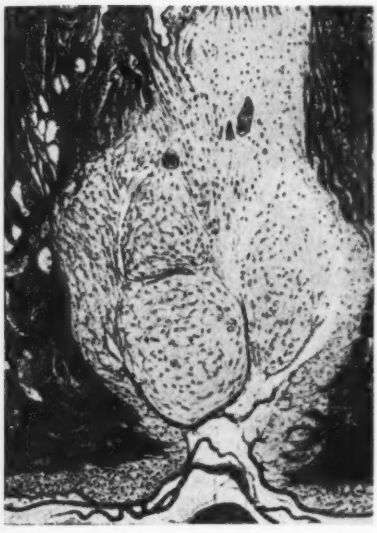

Fig. 1. Neuroma-like growths by a proliferation of the sympathetic nerve plexus in the appendix. This neuroma is brighter in contrast to its environment because of its large number of nuclei. Not only the sympathetic nerve tissue but also the muscular and connective tissue proliferate. 300X.—(Masson).

Fig. 2. Angioneuromatosis as described by Reubi (9) in case of neurogenic appendicopathy. Cross-section of lymphatic vessels and blood vessels, proliferating nervous tissue, and angioneuromatous proliferations of the blood vessels. 200X.—(Chiari).

rare in old age. However, we have found that the clinical picture of neurogenic appendicopathy often went unrecognized in old patients and that the symptoms were attributed to other illnesses. Whereas neurogenic appendicopathy, according to the opinion of European authorities (1, 6, 10), occurs in 7 to 17 per cent of all appendectomized cases, we have been able to find neurogenic appendicopathies in 50 per cent of all appendectomized patients over 60 years of age (3). This observation is easily explained by a simple chain of reasoning: Masson (8) found that more than 30 per cent of all obliterated appendices presented the picture of a neurogenic appendicopathy; Schweizer (11) even speaks of a percentage of 40 to 60; from Zuckerkandl (12) we know that in old age 37 per cent of all appendices are either totally or partially obliterated. Consequently neurogenic appendicopathy must occur more frequently in old age than in youth, and the obliterative form must be more frequent than the florid form of the disease.

SUMMARY

The histologic picture of neurogenic appendicopathy, which can also be recognized on macroscopic examination of the appendix, is described. The many clinical manifestations of the disease are enumerated and the gravity and extent of the disease discussed. Whereas some recommend appendectomy in all cases as the therapy of election, the author recommends appendectomy for old-age neurogenic appendicopathy only in those cases where organic changes are restricted to the appendix and all other complaints can be considered as reflexes of these changes. Where it is a manifestation of neurogenic enteropathy conservative treatment is recommended. Fifty per cent of appendices removed from patients 60 years or older show neurogenic appendicopathy by histologic examination.

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A RE-EVALUATION OF THE ORAL USE OF METRAZOL IN SENILE PATIENTS

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In a previous publication by the authors the results of the oral use of Metrazol (pentamethylenetetrazol, Bilhuber-Knoll Corp.) as a revitalizer in the geriatric population was evaluated (7). Using an objective behavior rating scale, no statistically significant differences were found in an experimental-control group design, using Metrazol in the amount of 0.1 Gm. t.i.d. for a period of 30 days. A review of the published literature available since 1952 reveals the fact that narrative, clinical reports continue to be written. Most of these publications report some sort of positive results (6). Carefully controlled evaluations, using "double-blind" techniques and objective criteria for measurement of behavioral changes, have often shown negative results (1, 2, 5).

The study to be described in the present report is the result of a careful re-evaluation of our own previous results, attempting to incorporate some of the suggested improvements (7, p. 101). The major recommended changes in that study were as follows: a) that the drug be given over a longer period of time, b) that increased dosage be used, c) and that a rating device more sensitive to behavioral changes *within* the psychiatric hospital environment be used.

MATERIAL AND METHODS

The patients for the study were selected from a female geriatric ward housing approximately 150 women over the age of 65 years. The patients were selected using the following criteria: 1) All patients were 65 years of age or older; 2) All patients fell into one of the following diagnostic categories—Chronic Brain Syndrome with Cerebral Arteriosclerosis or Chronic Brain Syndrome with Senile Psychosis; 3) An evaluation by the nursing staff indicating that the oral administration of the drug could be accomplished.

From the group of patients meeting these criteria 60 subjects were randomly selected and randomly divided into 2 groups—an experimental group and a control group.

All patients were evaluated through the use of the Ferguson Hospital Adjustment Scale (HAS) (4) within 1 week prior to the beginning of the administration of the drug. Ratings were independently made by 2 nurses who were thoroughly familiar with both the patients and the rating device. When the patients had been divided into 2 groups, their group identity was placed in the custody of the hospital superintendent and only he had access to this information. Each of the 60 patients received their drug dosage from a separate container marked only with the subject's name and a code number. (Although this process considerably increased the burden on the nursing personnel, it was considered necessary in order to eliminate the so-called band-wagon effect. In previous studies evaluating drug effects, it has been noted that once a subject identifies with a group he often tends to imitate the group feeling. This present design eliminates the possibility of the patient knowing that he belongs to any group at all.)

All patients in the study were given Metrazol in the following dosage for a period of 30 days: Experimental group—two 1½ gr. tablets t.i.d.; control group—identical placebo tablets t.i.d. (the placebos were supplied by Bilhuber-Knoll Corp.). At the end of 30 days the subjects were evaluated with the Ferguson HAS scale in the same manner as at the beginning of the study. At this time the drug dosage was increased to three 1½ gr. tablets t.i.d. At the end of a second period of 30 days the patients were re-evaluated on the same scale and the administration of the Metrazol was terminated.

RESULTS

The 3 sets of ratings were tabulated and compared to determine the existence of any differences between the experimental and control group. The HAS rating scale used contains 4 separate evaluations as follows:

I. Communications and interpersonal relations.
II. Care of self and social responsibility.
III. Work activities, and recreation.
IV. Total score.

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The authors wish to acknowledge the assistance of Clemmer Wait, Research Analyst, for application of statistical techniques in this research.

TABLE 1. T-VALUES OF SIGNIFICANCE TESTS BETWEEN MEANS OF EXPERIMENTAL AND CONTROL GROUPS RECEIVING METRAZOL AND PLACEBO THERAPY IN A FEMALE GERIATRIC HOSPITAL WARD.

Evaluations	Initial (I	Midpoint I + 30 days	Final I + 60 days
I. Communications and Interpersonal Relations	.69	.58	.24
II. Care of Self and Social Responsibility	.01	.67	.51
III. Work, Acitivties, and Recreation	.22	.26	.47
IV. Total Score	.19	.44	.03

The T-value must be 2.01 or greater to be significant at the 5% level.

The primary purpose of this scale is "to provide, with a minimum of expended time and special study, a quantitative estimate of the hospital adjustment of psychiatric patients. This estimate is based upon the actual behavior of the patients" (4. p. 3). It is believed that the standardization, clarity, and understandability of this scale makes it of considerable value for use in the behavioral measurement of any hospital patients.

The data were subjected to the usual t-test of significance (3, p. 216) to determine the significance of any changes between groups or within the group itself during the 60-day period. (It is to be noted that group I was reduced in size from 30 to 26 subjects because of illness or lack of cooperation of certain subjects during the experiment. Group II was reduced from 30 to 28 subjects for the same reasons.)

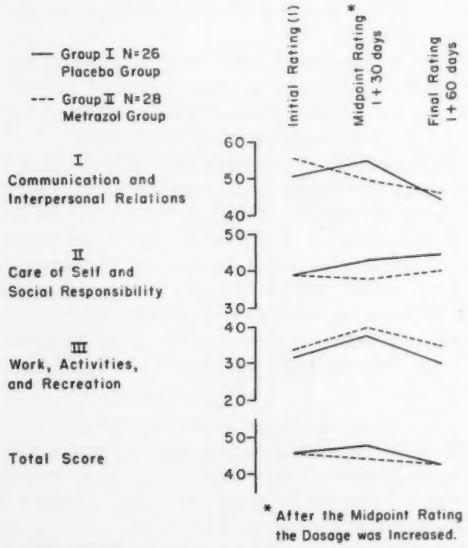

Fig. 1. Mean Ferguson HAS Scores of Experimental and Control Groups Receiving Metrazol and Placebo Therapy in a Female Geriatric Hospital Ward.

The general effects of the drug as determined by the Ferguson HAS scores are found in table 1 and figure 1. Table 1 lists the t-values of significance tests of difference between the means of the experimental and control groups. It is to be noted that none of these t-values even approaches a 5 per cent significance level at either the initial, the midpoint, or final rating in any of the 4 areas. Figure 1 graphically demonstrates the magnitude of change in the 2 groups at the 3 points in all 4 areas. These changes show no specific trends and are obviously not significant in magnitude.

DISCUSSION

It is our general impression that Metrazol in the amounts administered does not have any measurable effect upon geriatric patients' behavior. It is believed that the scale used is quite sensitive to behavioral changes *within* the hospital environment. There seems to be no significant value in increasing the dosage of Metrazol from 3 gr. t.i.d. to 4½ gr. t.i.d. This objective evaluation, therefore, must be considered as supportive evidence of negative results obtained in a previous study using a smaller dosage and a different rating technique. These results demonstrate no measurable evidence for continued use of Metrazol on a geriatric ward in a state mental hospital.

SUMMARY

Twenty-eight female geriatric patients in a state mental hospital were given oral Metrazol two 1½ gr. tablets t.i.d. for a period of 30 days and subsequently three 1½ gr. tablets t.i.d. for a second period of 30 days. An equivalent control group received an identical placebo tablet in the same dosage.

All patients were evaluated through the use of the Ferguson HAS rating scale by 2 independent raters at the beginning of the research, at the period of increased dosage, and at the termination of the treatment. No statistically significant differences were found in comparison of any of the ratings.

It was concluded that Metrazol in the amount indicated does not objectively change the behavior of a group of female geriatric patients in a state mental hospital.

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BOOK REVIEWS

ALTER UND KRANKHEIT, edited by W. Doberauer. Gesellschaft zur Förderung wissenschaftlicher Forschung, Vienna, 1957, 353 pages.

The publication "Alter und Krankheit" is an edited collection of papers presented at a postgraduate course in geriatrics held in Bad Hofgastein in Austria in March, 1956, under the auspices of the Austrian Geriatric Society. Twenty-two of the 30 chapters in the book deal with problems related to internal medicine, surgery and biology, 3 with psychologic aspects of aging, 1 with social conditions, and 4 with the therapeutic results obtained at the sanitarium "Bad Hofgastein."

Several of the papers concerned with aspects of medical and surgical diseases in old age are of a high quality and should be of special interest to American readers since they contain observations and descriptions of symptomatology which are not found in most Anglo-saxon textbooks. The presentation in these chapters is conservative and well balanced, and the statements are obviously based on extensive clinical experience by the authors.

The book does not contain any bibliographies, but literature references are available to readers on request.

This Austrian publication in the reviewer's opinion represents a valuable addition to the existing geriatric literature.

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St. Louis

EXPERIMENTELLE ALTERNSFORSCHUNG — EXPERIMENTAL RESEARCH ON AGING, edited by F. Verzár, Birkhäuser Verlag, Basel and Stuttgart, 1956, 290 pages, $8.50.

This book consists of the proceedings of a conference sponsored by the European section of the Biological and Medical Research Committee of the International Association of Gerontology in Basel, April 4, 1956. The conference was organized by J. F. Danielli, the chairman, and F. Verzár, the secretary of the European Committee. A total of 40 papers was presented, 23 in English, 13 in German, and 4 in French. In general the papers are pertinent, deal with experimental findings and are remarkably free of speculation. They are often technical, and since a great many fields are represented, the reader may encounter some difficult sections. Some of the data presented, while previously published in European journals, were not readily available in this country. The book undoubtedly gives an excellent picture of current European thinking concerning experimental approaches to the aging problem. About the only groups which may feel slighted are the classical biologists and workers interested in the interpretation of longevity tables.

The first 4 papers by Tunbridge; Hall; Banga, Baló, and Szabó; and Verzár deal with the changes which occur in collagen and elastin during maturation and senescence. The discussion between the speakers and other participants, such as W. Kuhn's, seems in keeping with the purpose of such a conference. Acceptance of the concept of the conversion of a portion of the collagen molecule into elastin would probably meet more resistance if a similar conference were held in the United States. Other papers describing changes in connective tissue during maturation and senescence are Joseph and Bourlière's paper on dilution potentials and the density of the colloidal charge in skin, Haranghy, Rácz, Hársfalvy, and Király's paper on sclerosis of the spleen, and Freydberg-Lucas and Verzár's study on the turnover of Ca^{45} in the skeleton, aorta, and lungs of mice.

Over-all changes in chemical composition of mice with aging are given by Brull and Keil, while water distribution in the aged is correlated with cardiac and renal function by Olbrich and Woodford-Williams.

Bürger gives data on the water, protein, neutral fat, cerebroside, phosphatide, and mineral composition of human brain at different ages. Divry discusses evidence for cerebral amyloidosis in senility. The disappearance of cochlear ganglia in older subjects is described by Fleischer, while Hügin and Verzár find that older rats do not maintain normal body temperature in a cold environment. Changes with age in the speed of information intake, discrimination, and learning are reported by Crossman and Szafran, and by Welford.

Problems related to atherosclerosis in the aged are discussed by several investigators. Schulz contrasts the composition and properties of arteries from leukemic and normal individuals of several age groups; Schettler compares changes in serum lipids with age with the changes observed following the ingestion of butter. Greppi, Scardigli, Salvini, and Guidi report on changes in plasma proteins and lipoproteins in young, old, and atherosclerotic subjects on several diets. Antonini compares the heparinoid substances and glycoprotein of the serum of normal and atherosclerotic subjects, 40 to 70 and 70 to 100 years of age. Schulz finds that plasma fibrinogen levels tend to increase with age and show an altered response during recovery from pneumonia. Nöcker observes a decrease in serum albumin and an increase in serum globulin with age. Geill discusses the relationship of pulmonary thrombosis, embolism, and cirrhosis of the liver.

Schulze estimates the protein and caloric requirements of human subjects of various ages. Rechenberger measures serum iron, serum iron binding capacity and ferratin content of various organs as a function of age. Senile degeneration in the kidneys of mice as indicated by proteinuria is discussed by Thung.

The diminished carbohydrate tolerance of later life is described by Baur. The use of vitamins in the treatment of mentally disturbed older patients is discussed by van der Horst, and the use of both vitamins and hormones in maintaining the health of aged individuals is described by Schneider. Thung contrasts senile changes in mouse and human ovaries. Mühlbock reports the incidence of liver tumors in mice from parents of varying ages.

Korenchevsky introduces a section on autointoxication in gerontology with a review of the pertinent literature, and Huet comments on dehydration and peptidemia. Amino acid imbalance in the diet of mature animals is discussed by Fisher, followed by a paper by Di Macco on the toxicity of acetylcholine as a function of age.

Brückner, Gsell, Hügin, Batschelet, and Verzár describe plans for following changes in visual accommodation, vital capacity, and pulse wave velocity in individual subjects over periods of 10 to 20 years. Ludwig considers the problem of setting normal values for physiologic functions in aged individuals with particular reference to blood pressure.

Professor Verzár should be congratulated for preparing this volume and for the scientific contributions he has made to its contents.

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BOOKS RECEIVED

Alter und Krankheit, edited by W. Doberauer, Gesellschaft zur Förderung wissenschaflicher Forschung, Vienna, 1957, 353 pages, (reviewed in this issue, page 404).

Care of the Elderly Sick in General Practice, by W. Ferguson Anderson, T. and A. Constable Ltd., Edinburgh, 1957, 27 pages, paper bound.

Experimentelle Alternsforschung — Experimental Research on Ageing, edited by F. Verzár, Birkhäuser Verlag, Basel—Stuttgart, 1957, 290 pages, $8.50 (reviewed in this issue, page 404).

Foot Troubles, by T. T. Stamm, Philosophical Library, Inc., New York, 1957, 122 pages, $4.75.

It Pays to Be Healthy, by Robert Collier, Prentice-Hall, Inc., Englewood Cliffs, New Jersey, 1957, 285 pages, $4.95.

Methodology of the Study of Ageing, Ciba Foundation Colloquia on Ageing, volume 3, edited by G. E. W. Wolstenholme and Cecilia M. O'Connor, Little, Brown and Co., Boston, 1957, 202 pages, $6.50.

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Regulation and Mode of Action of Thyroid Hormones, Ciba Foundation Colloquia on Endocrinology, Volume X, edited by G. E. W. Wolstenholme and Elaine C. P. Millar, Little, Brown and Co., Boston, 1957, 311 pages, $8.50.

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NON-VERBAL AND VERBAL PERFORMANCE IN NORMAL OLD AGE, SENILE DEMENTIA, AND ELDERLY DEPRESSION

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Two important, but opposing assumptions are often made concerning senile dementia. First, that dementia is an inevitable stage in the normal aging process to which everyone must come should they survive. The second assumption is that dementia is characterized by intellectual deterioration as classically shown in organic impairment. If the latter is the case, it is implied that dementia patients should show losses of ability over and above that due to normal aging and presumably independent of it. Recent studies (23) also stress the incidence of depression in elderly people, making another grouping to be considered in relation to the aging process.

What are the data concerning intellectual functions that are here relevant? Details are available (22, 26, 33) of the variations of non-verbal and verbal test performances with normal aging. Non-verbal tests may be considered as assessing the capacity to understand and apply a fresh method of thinking and therefore to acquire new knowledge. Verbal tests, on the other hand, seem to be measuring the general level of a person's intellectual attainments as a result of intellectual activity in the past. These two functions are essential to intelligent behavior but need to be separately assessed.

When separately assessed, the general trend is that the level of non-verbal test performance increases during childhood up to the age of 14, remains constant for about 10 years, and then progressively declines with age. It has been suggested that the higher the intelligence, the less the decline with increasing age—it is among the less intelligent that the normal decline of intelligence with age is most pronounced, (18, 32). A related observation is that those whose intelligence is most exercised is most retained. However, this is not entirely true as in a recent study (21) of 100 normal people aged 60-89, using 6 of the Wechsler-Bellevue sub-tests, the deterioration level was found to be independent of the intelligence level or of educational influences.

The level of verbal performance, however, increases steadily until middle-age, and even in later years may show only a small decline. Results claiming a maintenance of intelligence with age (4) will often be found on examination to be due to the use of tests more heavily weighted with verbal than non-verbal factors. A difficulty here with the elderly is that several studies have suggested that verbal performance itself may become impaired with advanced age, but the wide range of definitions for any particular word render this impairment difficult to measure (1, 8, 9, 10, 34, 35).

An abnormal discrepancy (after allowing for normal age variations) between any person's performance on non-verbal and verbal tests has formed the basis for estimations of intellectual deterioration (3, 31, 33), the thesis being that organic conditions—and to a lesser degree, functional disorders—result in an impairment of non-verbal performance, whereas verbal performance remains relatively free from impairment.

Normative data, however, past the ages of 60-65 is essential if either of the noted assumptions concerning senile dementia are to be established. It is also difficult to make any generalization unless tests are employed which contrast non-verbal and verbal performances rather than those tests which combine them in varying proportions.

The most adequate normative study of old

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I wish to thank Dr. P. K. McCowan, Physician Superintendent, the Crichton Royal, for making possible this study. Examination of the normal group was undertaken as part of a general research project concerning problems of normal aging, financed by the National Corporation for the Care of Old People. Thanks are also due to Dr A. C. Tait, Director of Clinical Research, and Mr. J. C. Raven, Director of Psychological Research, the Crichton Royal, for valuable advice. I am also grateful to Mr. K. Smart and Mr. H. Stewart, of Glasgow University, for assistance in statistical computations.

people (12) has been with the Wechsler Adult Intelligence Scale, the successor to the original Wechsler-Bellevue. Details of the sub-test performances are given. They find a decline with advancing age of all sub-test scores, particularly of the performance scale. Of all 11 sub-tests the vocabulary is the least affected by increasing age, the block design the most. These two sub-tests are probably the purest measures of verbal and non-verbal performance respectively, in the Wechsler Scale.

A marked reduction in test scores can be readily demonstrated in dementia, particularly in non-verbal tests (10, 19, 25, 30), which contrasts with performances in affective disorders. Even so, normal aging features may be prominent, although it has been noted (7) with the Wechsler-Bellevue Scale that those sub-tests showing the greatest decline due to normal aging were not necessarily the sub-tests most able in differentiating dementia. In a review of relevant Wechsler-Bellevue studies, Dorken (13) in fact concludes that:

". . . it can be demonstrated by psychological tests that senile dementia is qualitatively as well as quantitatively different from the normal senescent decline, is independent of it, and probably superimposed on it."

METHODS

To help in the elucidation of these various problems, a comparative study has been made of the non-verbal and verbal performances of three distinct groups of elderly people—normally healthy, depressed, and demented.

The tests used were the Progressive Matrices and Mill Hill Vocabulary Scales. The former claims to be a non-verbal

"test of a person's capacity at the time of the test to apprehend meaningless figures presented for his observation, see the relations between them, conceive the nature of the figure completing each system of relations presented, and by so doing, develop a systematic method of reasoning."

The Mill Hill Vocabulary Scale (Oral Definitions Form) is a verbal test which claims to

"assess the best intellectual level a person has reached as the result of mental activity in the past, whatever his present capacity for intellectual activity may happen to be."

These two tests have been standardized together for children and for adults up to the age of 65. The Coloured Progressive Matrices, Sets A, Ab, B, used in this investigation are constructed to give, for children and elderly people, a wider dispersion of scores than the Standard Scale, and to make the test more suitable for use with persons who are for any reason sub-normal or impaired.

The two tests were given by the author to two groups of elderly patients and a group of healthly old people, comprising in all:

1)—25 patients with senile dementia, selected as suffering from no other mental abnormality, and not too demented to perform the tests. Senile patients who were completely incapable of performing a test, or those whose performances showed no more than a passive selection of answers, were excluded. The implication of this selection will be discussed later.

2)—24 elderly depressives, selected as having no symptoms other than those associated with affective disorders.

3)—(a) 32 healthy old people, 61-70 years of age, and (b) 19 healthy old people, 71-80 years of age, who were all volunteers from the Dumfries Old Folks' Social Club, except for 4 physically fit residents of an Old People's Home. It can be argued that being volunteers and members of a Club, they represent the better preserved section of old people. Alternatively, it can be argued that really well-preserved old people retain their former interests and have no need for such a special social outlet. In either case, however, they do represent a group of healthy elderly people who can be compared with the depressed and demented groups.

To assess each patient's maximum potential of intellectual ability, regardless of losses during performance caused by any possible fluctuation of ability, each person in groups 1 and 2 was given the Matrices test again after an interval of 5 or 6 days. Using a method which proved valuable in an earlier study (24), their performances on the two Matrices tests were plotted against the order of difficulty of the problems as shown in Graph IV of the Guide to the test (29). The most difficult problem correctly solved on both test occasions was used in locating the point of maximum potential, and the patient's non-verbal ability estimated accordingly.

RESULTS

The two clinical groups will be considered first. These differ significantly in age, non-verbal and verbal performance (table 1). The senile dementia group is distinctly older and does less well on both non-verbal and verbal tests. A fluctuation of non-verbal test performance is present in both groups, being more

marked in the patients with senile dementia. The seniles' maximum potential score on the Progressive Matrices is also higher than their actual performance and is more comparable to the depressives' actual score. The senile patient therefore seems to fluctuate in productivity more than the depressive, regardless of the senile's potentiality for observation and clear thinking. Even so, for this group, the over-all test-retest reliability is higher than that of the depressives. Perhaps this again indicates that the seniles are more effectively impaired than the depressed group, giving a consistently lower level of productivity.

The comparatively low correlation between the Progressive Matrices scores and the computed maximum scores in the senile dementia group, relative to the depressives, may again indicate the effect of a marked fluctuation of non-verbal test performance.

In neither of the two clinical groups is age connected with any of the three non-verbal estimates (table 2), a combined correlation remaining insignificant. It can be inferred, then, that the difference in age of the two groups does not directly account for the differences in non-verbal performances indicated in table 1.

What may be significant, however, is the decline of verbal performance with age for the senile dementia group. It would seem that this group shows a disruption of the ability to recall even the meanings of words used in everyday speech.

Turning to normal group A, there are no sig-

TABLE 1. MEAN SCORES AND STANDARD DEVIATIONS.

	Age	P. M. 1	P. M. 2	P. M. Max.	M. H. V. S.
Senile means (N = 25)	73.84	15.00	15.36	25.32	41.64
S. Ds	5.66	5.51	6.66	6.26	16.52
Depressive means (N = 24)	68.17	22.92	23.67	29.75	53.08
S. Ds	5.25	7.15	7.08	3.42	13.65
Normal A means (N = 32)	66.81	21.41	–	–	44.06
S. Ds	3.25	5.62	–	–	11.51
Normal B means (N = 19)	74.47	20.84	–	–	46.63
S. Ds	2.30	5.91	–	–	15.35

The following means are significantly different at an 0.01 level: between seniles and depressives (Age; P.M.1; M.H.V.S); between seniles and normals B (P.M.1; M.H.V.S.); between depressives and normals A (M.H.V.S.); between P.M.1, and P.M. Max. (Seniles; depressives). No further significant differences occur at an 0.05 level.

TABLE 2. INTERCORRELATIONS OF VARIABLES.

		Age	P. M. 1	P. M. 2	P. M. Max.	M. H. V. S.
Age	Senile		−.12	+.02	−.06	*−.55*
	Depressed		−.19	−.17	−.24	−.05
	Normal A		+.09	–	–	+.01
	Normal B		−.26	–	–	+.08
P. M. 1				*+.88*	*+.46*	+.15
				+.70	*+.76*	*+.64*
				–	–	*+.73*
				–	–	−.27
P. M. 2					*+.50*	+.04
					+.81	*+.65*
					–	–
					–	–
P. M. Max.						+.07
						+.56
						–
						–

All coefficients in italics are significant at an 0.05 level. Of these only the P.M.1/P.M.max., P.M.2/P.M.max. fail to be significant at an 0.01 level.

nificant differences in age and non-verbal performance between them and the depressives (table 1). The lower verbal mean for the normal group may reflect a real difference between the local and hospital populations regarding early educational and cultural facilities. On the other hand, a relatively high verbal mean may be a genuine depressive feature to be linked with depressive characteristics such as conscientiousness. Such a feature may be associated with the variations of non-verbal/verbal ratios which themselves can be correlated with personality types (20). However, comparison with the published norms of the vocabulary (27) suggests that it is the normals who are relatively low rather than the depressives who are relatively high. As far as non-verbal performance goes, a comparison with the appropriate norms (28) indicates the normals are averagely endowed.

With normal group B, although older and comparable to the seniles in age, there is no sign of a decrease in non-verbal or verbal performance compared with the younger normal group A (table 1).

For both normal groups, there is no correlation with age of non-verbal or verbal performance.*

The decline with age of verbal performance in the senile dementia group would therefore seem to be a characteristic feature of senile dementia.

In one respect, the normal group B has something in common with the senile dementia group that distinguishes it from the two younger groups. This is the absence of the usual positive correlation obtaining between non-verbal and verbal performance. (This result compares with the appropriate Wechsler correlation coefficient between the block design and vocabulary sub-tests (12) which decreases from +0.59 to +0.36 from age group 60 to 65, to the age group older than 75.) It would seem that in the over-70's individual variations in non-verbal performance do not correspond with individual variations in verbal performance.

With both clinical groups, even after allowing for fluctuant interference in performance, there is a definite inability to go on to the 6 most difficult Matrix problems which appear to demand a genesis of new material by the education of relations. In this, however, their performances are similar to those of normally healthy old people.

DISCUSSION

As a result of the careful selection of the patients and old people studied, the groups are necessarily small. For the same reason the results merit careful consideration. Any inference drawn must necessarily be tentative. Nevertheless they indicate a need for a fuller examination of the points made both as regards the selection of the groups studied, the tests used, and the conclusions reached.

In non-verbal productivity, the senile dementia group is definitely poorer in output than elderly depressed patients and normal people of the same age. This difference, however, is partly eliminated once allowance is made for fluctuation of performance.

The progressive decline with age of verbal performance in the senile dementia group suggests a profound disruption of the ability to direct and integrate mental activity whether to solve problems or even to recall relevant information. This may be related to what is apparent clinically in the dementing process of senility. If allowance is made for the relative smallness of the age range and for the varying quality of acceptable vocabulary definitions, this decline of vocabulary in the senile dementia group would be even more apparent.

The disturbance of non-verbal productivity that seems to be evidenced in its function fluctuation may also be a result of this general breakdown of organized mental activity in the senile dementia group. Inability to do the non-verbal tests at all (which resulted in the omission of certain senile dementia patients from the group studied), may in fact be due to so great an interference with the smooth functioning of non-verbal performance that no sustained performance is possible.

The breakdown of acquired verbal ability peculiar to the senile dementia group is not, however, in keeping with the widely accepted postulate that verbal performance provides a

* Doppelt and Wallace (12) in their standarization sample, found all Wechsler sub-test scores, even the verbal ones, to decrease with increasing age. This difference in results from those reported here may have arisen because the non-hospitalized group studied here intentionally did not contain the proportion of senile people which one might find in a geographically selected sample, such as that of Doppelt and Wallace's, which was derived from a dwelling unit basis. On closer examination of the Wechsler data, the sub-test mean scores do not noticeably decline until over 70, and for the vocabulary sub-test only markedly decline in the 70-74 age grouping. These features suggest the possibility that nil or slight losses of non-verbal and verbal performances may be exaggerated by the inclusion of more senile individuals. Such individuals would tend to be over 70 and to give the type of test performance found in the senile group studied here.

measure of the best previous level of intellectual functioning. This observation finds some support in Wechsler-Bellevue studies (14, 15) which tend to question earlier beliefs (33) that senile deterioration shows the same type of test performance as that given in organic impairment in younger people. We may even find that the decline of verbal as well as non-verbal performance is an important measure of senile deterioration.

The results obtained in the present investigation, in which different clinical conditions have been carefully separated, suggest that two assumptions concerning senile dementia fall short of exactitude: 1) Dementia may not be an inevitable stage in the normal aging process, 2) In true dementia, verbal as well as non-verbal deterioration may be an important factor.

1) In the present investigation there is no evidence that patients suffering from depression in old age present differences in non-verbal performance distinguishing them from normally healthy people of the same age. It rather emphasizes the need to keep affective disorders of the aged quite distinct from senile dementia.

From both groups of normally healthy old people, it is interesting to note that the steady decline of non-verbal test performance commencing in the middle twenties apparently slows down in the sixties. This agrees with a Wechsler-Bellevue finding (5) that the decrease in intellectual efficiency from 40 to 60 exceeds that occurring from 60 to 80. Factorial studies also show a change in factor make-up (6, 16, 17). Birren (6) concludes that the performance of the elderly is determined by "what they know rather than what new information they can elicit from the test situation."

Further changes of non-verbal performance that do occur in dementia would seem to be due to inconsistent productivity rather than to a further loss of potential. In other words, they are less consistent than either the normally healthy old people or the elderly depressives, whether they are attempting to think logically or to recall acquired information. In this way they may be likened more to children.*

2) The senile patients studied in this investigation differ noticeably from the normally healthy old people and from the elderly depressives in that their recall of acquired information is not only poor, but also steadily declines as age advances.

These findings have even greater significance when it is recalled that in scoring the Vocabulary test performance the crucial question was: "Can he explain the meaning of a given word in other words?" not "Does he appear to know, or once to have known, what it meant?"; and that senile patients incapable of performing tests were excluded from the sample. The group of senile dementia patients studied here were selected on predominantly behavioral criteria. It would be interesting and important to see if cases of definite organic injury in the elderly also show a disturbance of both non-verbal and verbal test performances. If they do, at what chronologic age of development stage does an impairment of verbal performance begin to be of importance?

Whatever the answer may finally prove to be, the results of the present investigation suggest that, at least for the age range under consideration, present methods of assessing intellectual deterioration need careful examination.

SUMMARY

Two independent tests of non-verbal and verbal performance, standardized up to the age of 65, the reliability and validity of which are known, were administered individually to carefully selected groups of 51 healthy old people, 24 elderly depressives, and 25 persons with senile dementia.

The results suggest that in all old people, but in individuals with senile dementia particularly, there may be a function fluctuation of intellectual ability.

Depression in old age does not seem to manifest any disturbance of non-verbal and verbal performance compared with normal old people of approximately the same age range.

A decline with age of verbal performance seems to be important in the senile dementia group, distinguishing them from the elderly depressives and from normals of approximately the same age range.

In senile dementia, verbal deterioration as well as non-verbal deterioration would seem to be the important features to assess.

* It is sometimes said that psychologic tests similar in nature to those used with younger people are unfair to the elderly. They exaggerate the limitations of age without indicating its compensations or advantages (2, 11). Although it may be agreed that we would like to be able to assess the advantages of age, it is necessary to trace the further trend of those abilities known to be so important in younger years.

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THE RELATIONSHIP OF TIME PERSPECTIVE TO AGE, INSTITUTIONALIZATION, AND ACTIVITY*

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The degree to which an individual relates his overt and covert behavior to the past, the present, and the future has been a comparatively untapped psychologic research area. In recent years, however, the problem area of time perspective has been the focus of more attention from psychologists. Time perspective may be defined as the psychologic past, present, and future as they exist for and influence the individual. The present paper reports an investigation into the nature of the time perspective of aged men and the relationship of these time perspectives to age, to institutionalization, and to activity.

SUBJECTS

Two groups each of 30 aged male subjects were used, an institutionalized group and a non-institutionalized group. Subjects of the institutionalized group were selected from county infirmaries in the state of Michigan. The chief criterion for commitment to the infirmaries was the inability of the men to provide their own financial support.

One-half of the institutionalized men were between 50 and 60 years old, and the second half were between 61 and 76 years old. The non-institutionalized group was composed of residents of the community, and these men were individually matched to the institutionalized subjects on the basis of age, education, and occupational strata.

METHODS

To determine the time perspectives of the subjects, two experimental procedures were utilized; a modified scale technique and a projective method.

The scale technique was developed by Eson (1) and modified for the purposes of the present research. The subjects were asked to tell the examiner items which would give a clear picture of the things they had thought about and had spoken about during the past week or two. They were urged to mention at least 40 items. Upon the completion of this task, the subjects were asked to think back to the occurrence of each thought or conversation and to determine its temporal focus. They were asked to rate each item in terms of past, present, or future. Individual percentages for the three temporal divisions were then determined. The results are presented in table 1.

The projective method to determine time perspective made use of five TAT cards. The usual directions for TAT administration, which demand that the subject include the three periods of time in his stories, were not given. Instead, the subjects were asked only to tell a story about the pictures.

The TAT cards were scored as follows: The responses given to each card were examined for temporal references, and percentages of past, present, and future responses were calculated. These percentages are shown on table 2.

Each subject was also given a personal data questionnaire asking, among other things, the nature and amount of weekly time given over to employment, hobbies, leisure time activities, and organizational work.

RESULTS

The results of both the time perspective scale and the TAT cards are shown to be significantly more concerned with the past and significantly less concerned with the future in the institutionalized group when compared to the non-institutionalized group.

For a more detailed comparison, each of the groups was divided (on the basis of age) into two sub-groups. The results of this division may be seen on table 3. Of the men living at home, the older ones were significantly more concerned with the past and significantly less concerned with the future than the younger men in their group. But it must be noted that both the older and younger men of the community group gave more future than past responses. While the older men gave more past

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TABLE 1. PROPORTIONS OF TEMPORAL RESPONSES TO THE TIME PERSPECTIVE SCALE.

		Institution Group Age 50–60 N 15	Institution Group Age 61–76 N 15	Total Institution Group N 30	Home Group Age 50–60 N 15	Home Group Age 61–71 N 15	Total Home Group N 30
Past	Mean	.062	.696	.679	.161	.339	.250
	S.D.	.089	.141	.120	.083	.107	.132
Present	Mean	.213	.234	.224	.228	.248	.238
	S.D.	.085	.107	.096	.093	.088	.090
Future	Mean	.125	.070	.097	.611	.413	.512
	S.D.	.065	.101	.088	.127	.071	.141

TABLE 2. PROPORTIONS OF TEMPORAL RESPONSES TO THE TAT CARDS.

		Institution Group Age 50–60 N 15	Institution Group Age 61–76 N 15	Total Institution Group N 30	Home Group Age 50–60 N 15	Home Group Age 61–76 N 15	Total Home Group N 30
Past	Mean	.199	.222	.210	.070	.051	.060
	S.D.	.138	.147	.141	.076	.046	.063
Present	Mean	.772	.755	.764	.626	.675	.651
	S.D.	.141	.163	.150	.112	.089	.150
Future	Mean	.029	.023	.026	.304	.274	.289
	S.D.	.049	.043	.045	.089	.170	.136

TABLE 3. INTERGROUP AND SUB-GROUP DIFFERENCES OF PROPORTIONS OF TEMPORAL RESPONSES.

	Time Perspective Scale Response Proportions						TAT Response Proportions					
	Past		Present		Future		Past		Present		Future	
	Diff.	t	Diff.	t	Diff.	t	Diff.	t	Diff.	t	Diff.	t
Institution Group Age 50–60 vs. Institution Group Age 61–76	.034	.76	.021	.57	.055	1.72	.023	.43	.017	.29	.066	.34
Home Group Age 50–60 vs. Home Group Age 61–76	.178	4.89**	.020	.58	.198	5.08**	.019	.82	.049	.87	.030	.59
Total Institution Group vs. Total Home Group	.429	13.18**	.014	.60	.316	13.61**	.150	5.24**	.113	2.85**	.223	10.02**
Institution Group Age 50–60 vs. Home Group Age 50–60	.501	15.39**	.015	.44	.486	12.78**	.129	3.07**	.146	3.02**	.275	10.08**
Institution Group Age 61–76 vs. Home Group Age 61–76	.347	7.47**	.014	.37	.343	10.39**	.171	4.19**	.080	1.48	.251	5.39**
Institution Group Age 50–60 vs. Home Group Age 61–76	.323	8.58	.035	1.05	.288	8.94**	.143	3.80**	.007	1.58	.245	5.23**

** Significant at the 1 per cent level or less.

TABLE 4. CORRELATIONS BETWEEN PROPORTIONS OF PAST AND FUTURE RESPONSES GIVEN TO THE TIME PERSPECTIVE SCALE AND WEEKLY HOURS OF ACTIVITY FOR THE TOTAL EXPERIMENTAL GROUP (N 60).

	Proportion of Past Responses		Proportion of Future Responses	
Weekly hours of work	r	−.82**	r	.70**
	S.E. r	.042	S.E. r	.065
Weekly hours devoted to hobbies	r pbi	−.64**	r pbi	.64**
	t	7.15		6.89
Weekly hours of organizational activity*	r pbi	.06	r pbi	−.14
	t	.283	t	.962
Total weekly hours of activity	r	−.86**	r	.84**
	S.E. r	.033	S.E. r	.039

* Data derived from the non-institutional group only.
** Correlations significant at the 1 per cent level or less.

responses than the younger men, the group living at home had a future orientation.

The older members of the institutionalized group placed more emphasis upon the past and less emphasis upon the future than the younger men of the group confined to institutions. However, these differences were not significant. The institutionalized group, as a whole, was a past-oriented group.

It seems, then, that older men dwell more upon the past than younger men. But this study has shown that although older men living in the community devote a large share of their thinking to the future, the picture is considerably different for institutional residents, who devote the major share of their thoughts to their past experiences. In fact, when making inter-group observations, it was found that the older men of the community group were far more concerned with the future than the younger institutionalized men.

Since significant differences were found between the temporal emphasis of the older and younger segments of the non-institutionalized population and significant differences were not found between the older and younger men of the institutionalized group, it was concluded that institutionalization exerts a leveling effect upon time perspective in the direction of the past. Residents of institutions surveyed in this experiment had practically no interest in their futures. In their thoughts and conversations they tended to dwell almost exclusively upon past experiences.

Activity was determined by the number of hours a subject spent at work, at a hobby, or in some form of organizational activity. The activity of the subjects was correlated with time perspective data. As can be seen on table 4, there are significant positive correlations between the number of hours devoted to work and/or hobbies and future emphasis on the time perspective scale. There are significant negative correlations between the above mentioned variables and past emphasis on the time perspective scale.

Significant correlations were not found between hours devoted to organizational activity and either past or future emphasis. This may be due to the following circumstances: (a) The number of hours devoted to organizational work constituted only a small fraction of the total number of hours of weekly activity; (b) Few of the individuals who belonged to organizations were leaders of their groups. Most of the subjects seemed to be passive rather than active members of their organizations. Their organizational work may not have been as important or as interesting to them as their work or their hobbies.

It seems that activity alone is not a correlate of time perspective. Also important is the interest in and the motivation for a particular activity.

DISCUSSION

It seems that institutionalization brings about certain personality changes. It has been found that institutionalized residents have a more restricted range of interests and are less happy and less well-adjusted than people who do not live in institutions. These personality differences are due, in part, to the fact that the institutional situation is often very unstimulating when compared to the active, unpredictable world in which the institutional residents lived prior to their commitment. The present study gives evidence to support the theory of personality change due to institutionalization. For although personality, *per se*, was not investigated, a specific personality variable (namely, time perspective) was studied; and with respect to this personality characteristic very significant differences were found between institutionalized and non-institutionalized elderly men.

The institutions observed in this study, with their dreary, monotonous routine and their social stigma, are not pleasant situations. If it were possible to radically change the institutional situation, desirable changes in social adjustment and time perspective might be ef-

fected. It does not seem practical, however, to bring about gross alterations in the institutional setting. How then may changes be caused in the behavior and feelings of institutional residents? In order to bring about changes, the individual's perception of his situation must be altered. In the institution with which the author is associated, we have found that this can be done through counseling and the initiation of an activity program. This activity program should not be designed merely to keep the older people busy. It should, rather, be a program through which the institutional residents are encouraged and allowed to do productive work which would give them both monetary return and a feeling of still being useful members of society. In any sort of an institutional work program it is not the work itself which is beneficial to the workers. The participants must be motivated to engage in a particular activity if they are to receive satisfaction from it. Motivation may serve to tie the present to the future and can bring about a better understanding of the present.

SUMMARY

Time perspective data was obtained on 60 men over 50 years of age. Half of the subjects lived in county infirmaries and half lived at home. Results obtained indicate: (a) The institutionalized group were more concerned with the past and less concerned with the future than the non-institutionalized (home) group; (b) The older members of each group were more interested in the past and less interested in the future than the younger members of each group; (c) Age, alone, does not seem to channelize time perspective toward the past, as does institutionalization; (d) Activities, such as work for financial return (occupation) or work for pleasure (hobby), were related to time perspectives which were future oriented while organizational activity had no relation to the time perspective an individual maintained.

REFERENCE

1. Eson, M. E.; *An Analysis of Time Perspective at Five Year Levels.* Unpublished Doctoral Dissertation, University of Chicago, 1951.

BOOK REVIEWS

RETIREMENT POLICIES UNDER SOCIAL SECURITY, by Wilbur J. Cohen. University of California Press, Berkeley and Los Angeles, 1957, 105 pages, $3.00.

This volume is a short history of the development of Old Age and Survivors Insurance in the United States, from its beginnings in 1935 to the most recent changes in 1956. It deals principally with the questions of age at retirement, disability benefits under OASI, and the retirement test, and discusses controversies over these points as well as cost estimates and comparisons of various combinations of these factors.

Nothing other than a contributory plan of old age insurance was ever presented, and no age other than 65 was seriously considered when the program began; this age was not the result of investigation or comparison with other systems, but apparently was based upon cost considerations. Cost was again the main consideration in reducing the retirement age for women to 62 in the 1956 amendments. From the first, OASI was considered in principle to be a public program giving a basic continuity of protection which could be expanded and supplemented by private retirement plans; it was not meant to be the sole income of a large number of retired persons. However, OASI has become more and more comparable to private plans advanced by insurance companies and employers, even to the actuarially reduced annuities for early retirement instituted in 1956; at present minimum benefits are close to subsistence level. Apparently the only thing preventing even greater flexibility and liberality in the program is the cost factor.

From 1939, every session of Congress saw a bill introduced to provide disability benefits under Social Security, but the 1956 amendments established the first operative administrative structure for such benefits. The disability provisions were added with no really adequate investigations which could predict experience with and cost of such benefits; since the first month for which disability benefits are payable is July, 1957, this experience is yet to be developed.

Experience has been accumulated on the proportion of eligible persons who have retired with OASI benefits since these began in 1940. The percentage of workers who retired at age 65, the earliest eligible age, more than doubled from 1940 to 1954; in 1954, 55 per cent of women and 43 per cent of men retired at age 65, compared with 22 per cent and 18 per cent, respectively, in 1940. Since 1940, the percentage of those eligible who were receiving benefits has steadily increased, and the percentage of those whose benefits are suspended because of employment has steadily decreased. Under the 1954 amendments, the retirement test was put on an annual basis, instead of a monthly basis as was formerly the case, and the annual exempt amount of earnings was increased from $900 to $1200; the retirement test does not apply to persons over age 72. In view of the trends mentioned above, we should expect an even larger percentage of eligibles to receive OASI benefits under the 1954 liberalization of the retirement test, for which experience figures were not available when Professor Cohen wrote.

Probably the most important factor in the evolution of OASI has been cost, although certainly social, physical, and moral considerations have been important. The establishment of an advisory council in 1956 to assemble relevant information, review experience, and state the points at issue prior to each future Congressional consideration of revisions should help see to it that OASI actually evolves to fit the needs of a changing society, and that it is not left to "just grow."

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UNION POLICY AND THE OLDER WORKER, by Melvin K. Bers. Institute of Industrial Relations, University of California, Berkeley, 1957, 87 pages, $1.00.

This small monograph reports some general trends and hypotheses concerning the balance between favorable and unfavorable effects of union activity upon the employment opportunity and pensioning of the older worker, as deduced from a study of 12 major unions in the San Francisco Bay area. The material presented is exploratory and tentative, rather than definitive, but interesting insights are advanced by the author. Among these are: (1) when the union has achieved considerable control over hiring, e.g., the printers, the longshoremen, the elderly union member is protected in his opportunities for employment, but the elderly nonunion worker is liable to find entry into the union barred; (2) the seniority system as a mechanism for controlling layoffs is primarily a device to insure security for the union itself; seniority also discriminates in *favor* of the elderly worker, but union insistence upon strict application of seniority may wane as the union becomes more secure in its position; (3) the insistence upon the standard rate constitutes a union "barrier" to the employment of the older worker, and generally union attitude toward lowering the standard rate or permitting downgrading of an elderly worker has been negative; (4) although union policy toward compulsory retirement is not uniform, in industries where an oversupply of workers seems to threaten job opportunities for younger workers or, on the other hand, where job security is quite high, early retirement is usually encouraged; if the union itself provides the pension, there is usually no compulsory retirement age, whereas if the pension is funded by management, the latter insists upon such a requirement. Pension programs secured by collective bargaining seem to have two important functions for the union: first, they serve as a solidifying force for the union, and secondly, they serve as devices to drain older workers out of the labor market. Pensions were a device used quite frequently by the union to deal with unemployment in the labor markets investigated in this study.

On the whole, union policy seems to favor the aged worker, although the benefits he receives are largely by-products of union policies aimed at the prosperity of the union membership as a whole and at the basic security of the union itself.

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WHAT SOCIAL SECURITY MEANS TO WOMEN, Women's Bureau, U. S. Department of Labor, Washington, D. C., 1957, 26 pages.

This small, clearly-written pamphlet outlines the existing Old Age and Survivors Insurance coverage, including the 1956 revisions, with special emphasis given to their bearing upon the woman worker, the woman employer, and female dependents of insured workers. It answers such questions as what work is covered, what is meant by "fully insured" and "currently insured," the benefits provided, the basis for the computation of benefits, and questions concerning disability benefits. The most important of the 1956 amendments, from the point of view of women, are (1) the reduction of retirement age for women to 62 years, and (2) the "drop out" provisions which allow up to 5 years to be disregarded in estimating average earnings upon which benefits are based, a provision of special significance since women frequently are not continuously employed. The pamphlet includes practical information on how to start a Social Security account, what to do when a woman changes her name through marriage and how to file an application claim for benefits.

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BOOKS RECEIVED

Aging in the Modern World, a study discussion series for adults, a handbook for group members, prepared under the direction of Clark Tibbitts and Wilma Donahue, 175 pages, paper bound; *Aging in the Modern World*, a book of readings, selections from the literature of aging for pleasure and instruction, compiled by Clark Tibbitts, 245 pages, paper bound; *Aging in the Modern World*, a guidebook for leaders, a series of adult study discussion programs, prepared by Clark Tibbitts and Wilma Donahue, 68 pages, multilithed, paper bound, University of Michigan, Ann Arbor, 1957, $3.00 the set.

Community and Institutions for Aged, by Loudell Frazier and Dorothy L. Gebhart, American Public Welfare Association, Chicago, 1957, 15 pages, paper bound, multilithed, 50 cents (10-24 copies, 10% discount, 25 or more copies, 20% discount).

Rebuilding Human Lives: The Rehabilitation of the Handicapped, Part One, Trained Rehabilitation Workers: How Much Are They Paid? A Comparison of Salaries with Other Occupations, The Seventh Company, New York, 1957, 64 pages, paper bound.

JOURNAL OF GERONTOLOGY

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Section C

Organization Section
Index to Current Periodical Literature
Author Index to Current Periodical Literature
Index to Volume 10

VOLUME 12, SECTION A OCTOBER, 1957 NUMBER 4

ORGANIZATION SECTION

Program

Tenth Annual Meeting of the Gerontological Society, Inc.

October 31, November 1 and 2, 1957

HOTEL CLEVELAND

Cleveland, Ohio

J. E. BIRREN, *General Program Chairman*
A. B. CHINN, *Local Arrangements Committee Chairman*

A. I. LANSING, Biological Sciences
H. S. SIMMS, Biological Sciences
J. T. FREEMAN, Clinical Medicine
WILMA DONAHUE, Psychological and Social Sciences
FLORENCE E. VICKERY, Social Welfare

General Theme: ***Assessment or Measurement of Factors Influencing Aging and Programs for Their Control***

Thursday, October 31

8:30-10:00	Registration and Committee Meetings
10:00-12:00	Biological Sciences Symposium: Assessment of Biologic Mechanisms in Aging
12:00- 2:00	Luncheon Meeting, Followed by Separate Meetings for Each Professional Section and the General Member Section of the Society for Business of Sections
2:00- 4:00	Papers, Four Concurrent Sessions
4:00- 6:00	Social Welfare Symposium: Assessment of Social Welfare Services for the Aging and Aged
8:00-10:00	Public Discussion: A Survey of European Gerontology

Friday, November 1

9:00-11:00	Clinical Medicine Symposium: Assessment of Health of the Aging
11:00-12:00	Films and Exhibits
2:00- 4:00	Psychological and Social Sciences Symposium: Assessment of Mental and Social Health of the Elderly
4:00- 6:00	Local Program, Films and Exhibits
6:00- 7:30	Reception and Social Hour
7:30- 9:30	Annual Banquet.

Saturday, November 2

9:00-11:30	Papers, Four Concurrent Sessions
11:30-12:30	Business Meeting

THURSDAY, OCTOBER 31, 1957

8:30-10:00 a. m.—Registration, Mezzanine Floor; Committee Meetings.

10:00 a. m.-12:00 noon

Biological Sciences Symposium: Assessment of Biological Mechanisms in Aging

Empire Room, Parlor Floor.

Chairman: A. I. LANSING, Department of Anatomy, University of Pittsburgh.

LANSING, A. I., Introductory Remarks.

HEILBRUNN, L. V., Professor of Zoology, University of Pennsylvania, Philadelphia. Colloidal Changes in Aging Cells.

ROCKSTEIN, M., Associate Professor of Physiology, New York University College of Medicine. Heredity and Longevity in the Animal Kingdom.

BENSUSAN, H. B., Assistant Professor of Biochemistry, Western Reserve School of Medicine, Cleveland. Does Connective Tissue Age?

Commentators: F. BOURLIÈRE, Professor, Laboratory of Physiology, Faculty of Medicine, Paris, France, and F. VERZÁR, Professor of Physiology, University of Basel, Basel, Switzerland.

12:00 noon-2:00 p. m.

Luncheon Meeting

Ball Room, Mezzanine Floor.

2:00 p. m.-4:00 p. m.

Papers, Four Concurrent Sections

Biological Sciences

Parlors 34 and 36, Parlor Floor.

Chairman: W. ANDREW, Bowman Gray School of Medicine, Winston-Salem, North Carolina.

2:00 p. m.

SISTER ST. VIRGINIA M. COTTER AND CHARIPPER, H. A.: Changes with Age in the Lymphoid Tissue of the Golden Hamster (Cricetus auratus).

2:15 p. m.

DUBY, A., LIEGEY, F., AND DURY, MURIEL: In Vitro Respiration of Aortic Tissue of Rabbits Administered Adrenal and Pituitary Hormones.

2:30 p. m.

WEXLER, B. C., AND MILLER, B. F.: Age as a Factor in A.C.T.H.-Induced Arteriosclerosis in the Rat.

2:45 p. m.

FOLDES, F. F., SHANOR, S. P., ERDOS, E. G., AND BAART, NORA: Influence of Age on Human Plasma and Red Cell Cholinesterase Activity.

3:00 p. m.

GREENBLATT, I. J., GITMAN, L., FISHER, J., AND GOLDFIEN, P.: Studies with Antioxidants in an Attempt to Lower the Serum Lipids of Humans and Rabbits.

3:15 p. m.

KNISELY, W. H., BARNES, R. H., AND SATTERWHITE, W. M., JR.: In Vivo Observations on the Bulbar Conjunctival Blood Vessels and Blood of Functioning People 60 Years of Age and Over.

3:30 p. m.

BONDAREFF, W.: Submicroscopic Morphology of the Aged Nervous System.

3:45 p. m.

STREICHER, E.: Age Changes in the Calcium and Magnesium Content of Rat Brain.

Clinical Medicine

Terminal Room, Parlor Floor.

Chairman: H. MULHOLLAND, Committee on Aging, American Medical Association.

FREEMAN, J. T., Foreword.

2:00 p. m.

HAMWI, G. J.: Tolbutamide in the Management of the Elderly Diabetic.

2:15 p. m.

WILLIAMS, G. D.: Serial Physical and Physiologic Tests as Criteria for Evaluation of Therapeutic Methods.

2:30 p. m.

GOODMAN, J. I.: Nutrition, Life Tenure, and the Incidence of Degenerative Diseases.

2:45 p. m.

CORDREY, L. J., AND CHRISTIE, J. H.: A Study of Osteoporosis in the Experimental Animal Employing Strontium 85.

3:00 p. m.

HULTGREN, H. N., AND CAUL, E.: The Effect of Paget's Disease upon the Cardiovascular System.

3:15 p. m.

HITCHCOCK, C., AND MURPHY, T. O.: The Outlook of Vascular Surgery Upon the Aged.

3:30 p. m.

COHEN, T., AND GITMAN, L.: Studies of the Gastro-intestinal Tract in the Aged.

3:45 p. m.

Discussion.

Psychological and Social Sciences

Empire Room, Parlor Floor.

Chairman: G. ALDRIDGE, School of Social Work, Michigan State University, East Lansing.

2:00 p. m.

BOTWINICK, J., BRINLEY, J. F., AND ROBBIN, J. S.: Modulation of Speed of Response with Age.

2:15 p. m.

VAN ZONNEVELD, R. J.: An Orientating Study of the Memory of Old People.

2:30 p. m.

BRITTON, J. H., AND MATHER, W. G.: Personal and Social Adjustment of Rural Older Persons.

2:45 p. m.

MCCRARY, J. S.: The Role, Status, and Participation of the Aged in a Small Community.

3:00 p. m.

POLLACK, M., KAHN, R. L., AND GOLDFARB, A. I., Cultural and Environmental Factors Affecting Complex Perception in the Institutionalized Aged.

3:15 p. m.

STAFFORD, J. W., AND VERNIER, CLAIRE, M.: Psychologic Factors Associated with Differential Patterns of Institutional Versus Community Living Arrangements in a Geriatric Group.

3:30 p. m.

CUMMINGS, ELAINE, AND DEAN, LOIS: Interaction Patterns in Age.

3:45 p. m.

FRIEDMAN, E., OLMSTED, D., AND FLINT, ANITA: Attitudes of Nursing Home Operators Toward Their Profession.

Social Welfare

Rose Room, Main Floor.

Chairman: W. M. BEATTIE, JR., Department of Sociology, Washington University, St. Louis.

2:00 p. m.

BING, LUCIA: A Golden Age Center—An Experiment in Public and Private Agency Cooperation.

2:15 p. m.

LEVY, MARCELLE G.: Factors Affecting the Selective Use of Social Clubs for Older People.

2:30 p. m.

YOUMANS, E G.: Leisure-Time Attitudes of Healthy Older Persons.

2:45 p. m.

VICKERY, FLORENCE E.: A Social Activities Center Evaluates Its Organizational Patterns and Methods of Work in Light of What It Has Learned About the Psycho-social Needs of Older People.

3:00 p. m.

WILSON, P. A.: Techniques Involved in the Counseling and Placement of Older Workers.

3:15 p. m.

Discussion.

Read by Title: MULVEY, MARY C.: Improvement of State Programs: A Challenge to Gerontology.

4:00-6:00 p. m.

Social Welfare Symposium: Assessment of Social Welfare Services for the Aging and Aged

Cleveland Room, Main Floor.

Chairman: J. P. ANDERSON, Executive Director, National Association of Social Workers, New York.

Discussants:

WINSTON, ELLEN, Commissioner, North Carolina State Board of Public Welfare. Criteria for Assessing Our Progress in the Provision of Social Welfare Services for the Aging and Aged.

MATHIASEN, GENEVA, Executive Secretary, Committee on Aging, National Social Welfare Assembly. Assessment of Services in the Public Agency Field as Seen by a National Committee.

FITCH, W., Director, Special Staff on Aging, Department of Health, Education, and Welfare. Assessment of Services in the Public Agency Field as Seen by a Federal Department.

BARRY, MILDRED, Director, Department on Work with Older Persons, Welfare Federation of Cleveland. Assessment of Community Services as Seen by a Community Welfare Council.

BRITTON, J. H., Chairman, Committee for Study of Adulthood, Pennsylvania State University. Assessment of Services for the Aged in Rural Communities.

Commentator: R. J. VAN ZONNEVELD, Coordinating Physician for Gerontological Research, National Health Research Council, T.V.O., The Hague, The Netherlands.

6:00-8:00 p. m.—Open.

8:00-10:00 p. m.

Special Symposium: A Survey of European Gerontology

Cleveland Room, Main Floor.

Chairman: R. J. HAVIGHURST, President of the Gerontological Society, Inc.

VERZÁR, F., Professor of Physiology, University of Basel, Basel, Switzerland. General Biology.

BOURLIÈRE, F., Professor, Laboratory of Physiology, Faculty of Medicine of Paris, Paris, France. Comparative Biology.

WELFORD, A. T., Lecturer in Psychology, Cambridge University; Fellow, St. John's College; Director, Nuffield Unit for Research on Aging, Cambridge, England. Psychological and Social Sciences.

VAN ZONNEVELD, R. J., Coordinating Physician for Gerontological Research, National Health Research Council, T.V.O., The Hague, The Netherlands. Public Health and Welfare.

GEILL, T., Medical Director, De Gamles By, Copenhagen, Denmark. Clinical Medicine.

FRIDAY, NOVEMBER 1, 1957

9:00-11.00 a. m.

Clinical Medicine Symposium: Assessment of Health of the Aging

Ball Room, Mezzanine Floor.

Chairman: W. A. SODEMAN, Professor of Medicine, Jefferson Medical College, Philadelphia.

SIMONSON, E.: Functional Capacities of Older Individuals.

LEAKE, C. D.: An Affirmative Approach to Clinical Education in Geriatrics.

MONROE, R. T.: The Mechanisms of a Geriatric Clinic and Its Place in the Community.

FARR, L. E.: Atomic Medicine in Geriatrics.

Commentator: T. GEILL, Medical Director, De Gamles By, Copenhagen, Denmark.

11:00 a. m.-12:00 noon

Films and Exhibits, Mezzanine Floor.

12:00 noon-2:00 p. m.—Open.

2:00-4:00 p. m.

Psychological and Social Sciences Symposium: Assessment of Mental and Social Health of the Elderly

Ball Room, Mezzanine Floor.

Chairman: WILMA DONAHUE, University of Michigan, Ann Arbor.

WELFORD, A. T., Cambridge University, Cambridge, England. The Stress of Work on the Older Individual.

KAPLAN, M., Boston University. The Stress of Leisure on the Older Individual.

MCCONNELL, J .W., Cornell University, Ithaca, New York. The Impact of Aging on the Economy.

TIBBITTS, C., Dept. of Health, Education, and Welfare, Washington, D. C. The Impact of Aging on Social Institutions.

Commentator: A. T. WELFORD, Cambridge University, Cambridge, England.

4:00-6:00 p. m.

Local Program; Films and Exhibits

Mezzanine Floor

6:00-7:30 p. m.

Reception and Social Hour

Ball Room, Mezzanine Floor

7:30-9:30 p. m.

Banquet

Ball Room, Mezzanine Floor

R. J. HAVIGHURST, President of the Gerontological Society, Inc. A World View of Gerontology.

SATURDAY, NOVEMBER 2, 1957

9:00-11:30 a. m.

Papers, Four Concurrent Sections Biological Sciences

Parlors 34 and 36, Parlor Floor.

Chairman: H. B. BENSUSAN, Assistant Professor of Biochemistry, Western Reserve School of Medicine, Cleveland.

9:00 a. m.

MORAN, T., AND LANSING, A. I.: Pseudoxanthoma Elasticum.

9:15 a. m.

PARK, HEE-YONG, KEARNS, J. E., TELOH, H. A., AND DAVIS, H. G. JR.: Changes in Morphology of the Thyroid Gland with Aging.

9:30 a. m.

FLEMING, H. S.: Variations in Aging of Cellular Components of Tooth Germ Transplants.

9:45 a. m.

ANDREW, W., AND MCCREIGHT, E. C.: The Reality of Age Changes in the Nervous System.

10:00 a. m.

SULKIN, N. W.: The Duration of Pigmentation in the Nerve Cell Following Prolonged Administration of Acetanilid.

10:15 a. m.

HIMWICH, WILLIAMINA A., COOMBS, ALAYNE, HAYNES, E. E., AND HIMWICH, H. E.: Longitudinal Study of the Effect of Aging in Man.

10:30 a. m.

BERG, B. N.: Diseases in Old Rats, Both Male and Female.

10:45 a. m.

ROGERS, J. B., AND ROGERS, J. H.: Factors Concerned with Longevity in Guinea Pigs.

11:00 a. m.

Discussion.

Clinical Medicine

Terminal Room, Parlor Floor.

Chairman: G. H. HUNT, Director, Center for Research on Aging, NIH, Washington, D. C.

9:00 a. m.

MCGAVACK, T. H., AND SEEGERS, WINNIFRED: Thyroid Patterns, Their Identification and Management After Age Sixty-Five.

9:15 a. m.

PESZCZYNSKI, M.: Contractures in the Hemiplegic Patient.

9:30 a. m.

CROMWELL, L. W.: Arthritis, Arthrosis, and Arthralgia in the Elderly.

9:45 a. m.

OBRIST, W. D., AND DOVENMUEHLE, R. H.: Relation of Blood Pressure to the Electroencephalogram in People Over Sixty.

10:00 a. m.

KOUNTZ, W. B.: Nutritional Consideration of the Older Person.

10:15 a. m.

BECK, C. S.: The Problem of Coronary Artery Disease.

10:30 a. m.

Discussion.

Read by Title: FRIEDMAN, O. L., AND FRIEDMAN, L. O.: A New Approach to the Clinical Classification of Senility.

KRAL, V. A.: Psychiatric Observations in an Old Peoples Home.

Psychological and Social Sciences

Empire Room, Parlor Floor.

Chairman: E. FRIEDMAN, University of Wisconsin, Madison.

9:00 a. m.

PRESSEY, S. L.: Jobs at Eighty.

9:15 a. m.

THOMPSON, W. E., AND STREIB, G. F.: Retirement and Health.

9:30 a. m.

BURGESS, E. W.: Attitudes to Aging and Retirement of Employees in Industries by Different Economic Levels.

9:45 a. m.

HUNTER, W. W.: Preparation for Retirement of Hourly Wage Employees.

10:00 a. m.

HAVIGHURST, R. J.: The Significance and Content of Leisure Activities from Age Forty to Seventy.

10:15 a. m.

SHANAS, ETHEL, AND MONSKY, SELMA F.: Interviewers' Attitudes in a Nationwide Study of Older People.

10:30 a. m.

TUCKMAN, J., AND LORGE, I.: The Projection of Personal Symptom into Stereotype about Aging.

10:45 a. m.

WEBBER, I. L.: Variations in Marital Status of the Older Population of the United States According to Residence and Region.

11:00 a. m.

NEUGARTEN, BERNICE L., AND GARRON, D. C.: The Attitudes of Middle-Aged Persons Toward Growing Older.

11:15 a. m.

KAHN, R. L., AND GOLDFARB, A. I.: Attitudes Toward Illness in the Aged.

Social Welfare

Rose Room, Main Floor.

Chairman: MARGARET WAGNER, Director, Benjamin Rose Institute, Cleveland.

9:00 a. m.

FERRARI, NELIDA A.: Group Work Programs in Homes for the Aged.

9:15 a. m.

REYNOLDS, MILDRED: Nutrition, A Factor in the Mental and Physical Health of Older People.

9:30 a. m.

GOLD, J. G., AND DRAY, M.: Nutrition and Special Diets in Homes for the Aged.

9:45 a. m.

REEVE, G. H.: Individualized Care of the Aged.

10:00 a. m.

GOLDBERG, RUTH L.: Family Homes for the Aging.

10:15 a. m.

Discussion.

Read by Title:

VAN ZONNEVELD, R. J.: Socio-medical Investigations for the Benefit of the Accommodation of the Aged.

11:30 a. m.

Business Meeting of the Gerontological Society, Inc.

Ball Room, Mezzanine Floor

Abstracts

All abstracts are edited by the respective Section Program Chairmen.

SECTION ON BIOLOGICAL SCIENCES

Abstracts edited by A. I. Lansing, Ph.D.

The Reality of Age Changes in the Nervous System.*

W. ANDREW AND C. E. MCCREIGHT, *Department of Anatomy, the Bowman Gray School of Medicine, Winston-Salem, North Carolina.*

Recent studies by various investigators have given largely negative results in relation to histologic and cytologic changes in the nervous system. In order to make a critical re-examination of this subject, *synchronous* staining has been employed in brain, spinal cord, and sensory ganglia of C57 Black mice. In this method paraffin sections from young (129-248 days) and senile (596-818 days) mice are mounted on the same slide and stained in a 1 per cent aqueous solution of Cresyl violet (Cresylecht Violet) at pH 4.8. Some 50 animals have been studied. The differences in staining are striking and clearly visible to the naked eye, sections from senile animals being invariably lighter than those of corresponding parts of the nervous system of young animals. Cellular details also are clearly different in the two groups of animals. Conspicuous are the vacuoles in motor cells of the spinal cord of senile mice. The effects of several different methods of fixation and preparation on these gross and microscopic age differences are discussed.

* Grateful acknowledgement is made of support of this work by a grant from the Josiah Macy, Jr. Foundation.

Diseases in Old Rats, Both Male and Female.

BENJAMIN N. BERG, *Department of Pathology, College of Physicians and Surgeons, Columbia University, New York.*

The histopathologic changes in the tissues of Sprague-Dawley rats over 950 days old are described in detail. Incidence and severity of lesions in the heart, blood vessels, kidneys, and skeletal muscles, and occurrence of tumors are compared in male and female animals. A marked difference is found between the sexes in susceptibility to these diseases, and the significance of this difference with relation to longevity and aging is discussed.

Submicroscopic Morphology of the Aged Nervous System.

W. BONDAREFF, *Section on Aging, Laboratory of Psychology, National Institute of Mental Health, National Institutes of Health, Public Health Service, U. S. Department of Health, Education and Welfare, Bethesda, Maryland.*

The light and electron microscopes are being utilized in a study of the spinal ganglia of aged Sprague-Dawley rats. Electron microscope data, derived from osimum fixed, sectioned material, is presented which indicates that intraneuronal pigment (lipofuscin) is not derived from degenerate mitochondria. It is suggested that pigment is associated with the Golgi complex and a mechanism of pigment derivation is proposed. Freezing and drying, adapted to electron microscopy, is being employed in an attempt to further elucidate the cytologic mechanism of pigment deposition.

In Vitro Respiration of Aortic Tissue of Rabbits Adminstered Adrenal and Pituitary Hormones.

A. DURY, F. LIEGEY, AND MURIEL DURY, *Dorn Laboratory for Medical Research, Bradford Hospital, Bradford, Pennsylvania.*

Several recent observations suggest that the metabolic behavior of aortic tissue might be an important factor in the development of atherosclerosis. Furthermore, recent studies have shown that hormones affect lipid metabolism and exert an influence on the metabolic activity of aortic tissue in vitro from intact and hormonally-treated rabbits. The O_2 consumption of the aortic arch (3 cm. from aortic ring) and the descending aorta was measured by standard Warburg-manometric procedures. The O_2 consumption by the two aortic regions were determined in buffer, buffer-glucose, buffer-succinate, and buffer-glucose-succinate. The animal groups (6-10 rabbits in each) were: Untreated controls, and rabbits killed 5 hr. after subcutaneously injected epinephrine in oil (1 mg./Kg.), cortisone acetate (10 mg./rabbit), or growth hormone (5 mg./Kg.). The Q_{O_2}/60 min. of the descending aorta of untreated rabbits was 50 per cent lower than the aortic arch in buffer and buffer-succinate. When incubated in buffer-glucose or buffer-glucose-succinate, the rate of respiration of the two aortic regions was the same. The aortic arch and descending aorta oxidized succinate at a rate of 5 times higher than the endogenous rate of the respective regions. Addition of glucose resulted in decreased O_2 consumption of the aortic arch to the extent of 40 per cent, while the Q_{O_2} of the descending aorta was not affected compared with the endogenous rate. These data indicate that there is a considerable difference in respiratory activity between the aortic arch and descending limb of aorta of intact rabbits in endogenous metabolism, but both regions have a similar capacity to oxidize succinate. Since addition of glucose to aortic arch incubates (but not descending aorta) depressed the respiration of this tissue the obvious inference is that glucose supplementation permitted this region to obtain more of its energy from glycolysis. The endogenous Q_{O_2} of the aortic arch of epinephrine-injected rabbits was decreased 13 per cent, cortisone-injected was depressed 27 per cent, and growth hormone-injected 65 per cent compared with controls. The implications of these and other results in different incubation media of aortic regions of hormonally-treated rabbits will be discussed.

Variations in Aging of Cellular Components of Tooth Germ Transplants.

H. S. Fleming, *Research Associate, Department of Pathology, Yale University School of Medicine, New Haven, Connecticut.*

Anlagen of teeth survive both homo- and heterotransfer to selected locations in laboratory animals where they rapidly form mature tooth structures. Cellular components of such transplants then undergo aging and/or degenerative changes. Pulpal areas become avascular and acellular with osteoid tissue ultimately replacing both pulp and dentin. After formation of the enamel matrix, cells of the inner enamel epithelium undergo degenerative changes as keratin, their end product, is produced.

Aging and/or degenerative changes may be accelerated under several experimental conditions so that expected formation of enamel and dentin is retarded, minimized, or fails to take place due to alterations in the biologic behavior of certain cells. These fêted cells rapidly age and degenerate on failure to produce mineralized components of teeth. It is also important that under several other experimental conditions aging and/or degenerative processes can be delayed so that greater amounts of enamel and dentin may be formed. In such instances cells remained numerous, young, and viable for longer periods than was observed under other conditions. This was evidenced by a high degree of cellularity and vascularity in pulpal areas and an increase in the numbers of inner enamel cells actively forming enamel matrices. Thus, failure to age resulted in development of huge explants.

Influence of Age on Human Plasma and Red Cell Cholinesterase Activity.

F. F. Foldes, S. P. Shanor, E. G. Erdos, and Nora Baart, *Department of Anesthesiology, Mercy Hospital and Section on Anesthesiology, Department of Surgery, University of Pittsburgh.*

It has been shown previously that there is a significant sex variation between the plasma cholinesterase (PChE) activity of young healthy adult male and female subjects (*Fed. Proc. 15:* 482, 1956). No such sex variation was found in red cell cholinesterase (RChE) activity. In the present study of the PChE and RChE activity of 25 male and 25 female hospital patients of over 70 years of age was investigated with Ammon's modification of the Warburg manometric method using acetylcholine (ACh), succinylcholine (SDCh) and procaine (Proc.) substrates. Heparinized blood was centrifuged and the plasma separated from the red blood cells. The red cells were washed and hemolyzed. The PChE levels of these patients are compared with those of young adults of both sexes. There is no significant difference between the PChE and RChE activity of old males and old females. The PChE activity of males over 70 is significantly lower than that of young adult males. There is no age variation in the PChE activity of females.

Studies with Antioxidants in an Attempt to Lower the Serum Lipids of Humans and Rabbits.

I. J. Greenblatt, L. Gitman, J. Fisher, and P. Goldfien, *Messinger Research Laboratories, Beth-El Hospital, Brooklyn.*

A group of 9 human males and 12 female rabbits were studied with antioxidants (ascorbic acid, d-alpha tocopherol acetate (Eastman Kodak), Dalpac, FG (Hercules Powder), and/or isoascorbic and ascorbic acids. The diets were kept constant, in both human and animal subjects. The animals were divided into 3 groups of 4 in each group; group I with 0.75 per cent cholesterol (in peanut oil) of the diet; group II, a normal rabbit group, on a regular chow diet, and group III with 75 per cent cholesterol (in peanut oil) plus the tocopherol. The rabbits were kept on this diet for two months.

After a control series of bleedings, serum cholesterol and ultracentrifugation analyses of lipoproteins were carried out at biweekly intervals. The d-alpha tocopherol was ingested at a level of 500 to 600 mg./Kg. in man and animals, per day. The butylated hydroxytoluene was given in varying doses from 450 mg. per day to 1350 mg. per day. Ascorbic acid was given in combination or singly. The massive doses of tocopherol in humans produced a fall in the S_f 0-10 by as much as 18 per cent, and in the cholesterol levels by as much as 30 per cent. No deleterious effects were noted by any of the compounds or combinations. Subjects on alpha tocopherol on a 500 to 600 mg. dose per day for as long as 5 months did not show any side reactions. The hypercholesterolemias responded best to the alpha tocopherol. Butylated hydroxytoluene increased the cholesterol levels in some human subjects by as much as 25 to 30 per cent.

Rabbits receiving the cholesterol and vitamin E showed a delayed rise in serum cholesterol when compared with rabbits on cholesterol without vitamin E.

Longitudinal Study of the Effects of Aging in Man.

Williamina A. Himwich, Alayne Coombs, E. E. Haynes, and H. E. Himwich, *Thudichum Psychiatric Research Laboratory, Galesburg State Research Hospital, Galesburg, Illinois.*

A longitudinal study of the biochemical effects of aging on the metabolism, physiology and psychologic responses of 12 schizophrenic male patients of approximately 55 years of age and 13, high-grade, male, mental defectives in the same age group has been initiated. Routine determinations made at 6-12 month intervals include blood chemistry, urinalysis, basal metabolic rate, and protein-bound iodine. In the physiologic field the routine tests measure ECG, vital capacity, Schneider index, pulse, pulse pressure, back and hand strength, auditory and visual acuity. Basic psychologic testing is made with the Rorshach, the Wechsler-Bellevue, memory span, and manual dexterity tests.

Period X-rays of the hand and of the oscalcis are checked with a densitometer to determine calcification. Pictures of the patients in the nude are taken against a grid every year to permit the evaluation of body build, posture, and stance.

The subjects have now been followed for about three years. The data to date permit only the establishment of base lines for each patient. The basic organization and philosophy of this reasearch will be discussed.

In Vivo Observations on the Bulbar Conjunctival Blood Vessels and Blood of Functioning People 60 Years of Age and Over.*

W. H. KNISELY,† R. H. BARNES,‡ AND W. M. SATTERWHITE, JR.,§ *From the Departments of Medicine, Anatomy, and Psychiatry, Duke University School of Medicine, Durham, North Carolina.*

The purpose was to observe microscopically the systemic blood and blood vessels of the 60-year and older functioning people being studied at Duke, and to relate any findings to other data. Other parameters studied include: EEG, routine hematologic work, and neurologic, sensory, social, psychologic, psychiatric, and physical status.

Light was shone on the conjunctiva and the area studied microscopically with 16 to 150 X magnification (see Glasser's *Medical Physics*, Vol. 2; p. 129). Observations and photographs were made before and after topical 10 per cent neosynephrine. Circulatory factors quantitatively estimated from 0 to ++++ included, number of vessels per unit area, venous tortuosity, sacculations, arterial- and venous - agglutinated blood, and stasis. A numerical Index was made.

Over 150 people have been studied and observations related with other paramcters in the first 80. The Index related with age better than did any single vascular factor. Only 4 subjects were considered healthy normal by all criteria for vessels by Clark and Clark, 1935, and for vessels and blood by Brooks, et al, 1950. All but 5 had some venous tortuosities. The outside portions of the curves of tortuous veins tended to be saccular, and these and other sacculations failed to constrict with 10 per cent neosynephrine; thus, wall irregularities were accentuated.

The criteria for healthy normal blood and vessels must be revised for this age group, or, some of these observations must be considered vascular pathology. Because the circulation in 4 individuals was healthy normal by all criteria for young, and, because the Index related with age, these findings are considered pathology related to age.

* This investigation was supported by a research grant from the National Institute of Mental Health of the National Institutes of Health, United States Public Health Service.

† This work done during the tenure of an American Heart Association Research Fellowship.

‡ Present address is: The Greater Kansas City Mental Health Foundation, Kansas City, Missouri.

§ Supported by a Tobacco Industry Student Research Fellowship.

Pseudoxanthoma Elasticum.

T. MORAN, AND A. I. LANSING, *Departments of Pathology and Anatomy, University of Pittsburgh.*

The involved skin area from a typical clinical and histologic example of pseudoxanthoma elasticum has been studied by elastase digestion and electron microscopy. The results of both studies strongly support the viewpoint that the primarily altered fibers in this disease are derived from elastic tissue. There is also a definite increase in collagenous tissue in the involved areas. This is regarded as a secondary change possibly arising in response to the primary elastic tissue alteration or the calcification. This concept of the pathogenesis of the disease may resolve some of the discrepancies previously reported on the nature of the involved fibers in pseudoxanthoma elasticum.

The Changes in Morphology of the Thyroid Gland with Aging.

HEE-YONG PARK, J. E. KEARNS, H. A. TELOH, AND H. G. DAVIS, JR., *Departments of Pathology and Surgery, Evanston Hospital Association, Evanston, Illinois, and Northwestern University Medical School, Chicago.*

Morphologic changes associated with aging in human thyroid glands were studied with necropsy material obtained at the Evanston Hospital over the period 1953 to 1955. The results were recorded with detailed description of changes occurring in each element of the thyroid gland.

The primary object of this study was to observe how nodules are formed in the thyroid gland with the aging process and in what points they are basically different from the true adenoma. In this regard, the term pseudo-adenoma has been introduced in place of the rather misleading complicated old terms—colloid, follicular, Hurthle cell, papillary fetal, and/or embryonal nodules. One exception to this is that when the latter two types, papillary and fetal, occur as a solid form in the younger age groups, it may be a true adenoma or potentially malignant tumor and must be considered separately.

In this series, nodules in the thyroid gland were found in 75 per cent of all cases; none of them showed any evidence of clinical thyrotoxicosis or histologic picture of neoplasm.

In persons beyond 50 years of age, the incidence of nodules in the thyroid was 84 per cent and was predominant in the females.

Steps to the formation of pseudo-adenoma have been illustrated and discussed in the light of connective tissue proliferation, hyperplasia and involution of the follicles, and other factors, all of which may occur during the process of aging.

The so-called solitary nodule, lymphocytic infiltration and arteriosclerosis have been briefly discussed.

Factors Concerned with Longevity in Guinea Pigs.

J. B. ROGERS AND J. H. ROGERS, *Department of Anatomy, University of Louisville School of Medicine.*

The longevity of guinea pigs in the colony maintained for the study of various phases of aging will be reported. Our observations cover about 16,000 animals. We have been concerned with two major factors connected with survival—inheritance and environment. We have used the last litter of an old female as breeding stock to increase longevity. In regard to environment and diet, we changed from oats to pellets in 1953 when the alfalfa hay available was of poor quality. Since 1955 part of the colony was maintained at a summer minimum of 83 F. Another part of the colony has not been mechanically cooled. Other features of our maintenance have remained unchanged.

In our report of April, 1949, on the period between July 1, 1941, and January 1, 1949, the average age of females at death was 547 days and of males 947 days.

In the period between January 1, 1949, and January 1, 1957, there has been little change in the survival time of 601 days for the females and 875 days for the males.

Since environmental factors have been relatively constant and the routine of breeding continued unchanged, it seems that long life is a strain characteristic.

Changes with Age in the Lymphoid Tissue of the Golden Hamster (Cricetus auratus).

SISTER ST. VIRGINIA M. COTTER AND H. A. CHARIPPER, *Department of Biology, Graduate School of Arts and Science, New York University.*

The spleen, thymus, axial and deep cervical lymph nodes of 31 golden hamsters from 13 days to 94 weeks were studied. The steady decrease in white pulp area after 20 weeks of life is a constant feature of the aging spleen of the hamster. White pulp is far more labile than red, in which regressive changes and chiefly fibrosis occur only in old age. The thymus of the hamster reaches its peak development shortly after puberty. It maintains a high mitotic rate longer than the spleen but shows cessation of Hassall corpuscle formation and erosion of the cortex—at the same age as beginning involution of the splenic white pulp.

Thymic lymphocytes and thymic reticular cells reach their maximum development and undergo involution at the same time. Quantitatively, the cortical area diminishes first and to a greater extent than the medulla. Disappearance of Hassall's corpuscles parallels regressive changes in the lymphatic tissue. The deep cervical and axial nodes show a similar regression of their lymphocyte components at the same time and differ only in the extent of fibrosis. The axial nodes undergo fibrosis and metaplastic changes in old age; deep cervical nodes undergo little fibrosis, but instead age by a thinning out of the lymphocytes and an extreme extension of the medulla at the expense of the cortex.

Aging changes throughout the lymphatic tissues are similar in the hamster. They are 1) decline in mitotic rate, 2) disappearance of germinal centers, 3) reduction of the area of and/or a thinning out of lymphocyte-bearing stroma, and 4) hypertrophy of connective tissue. There is an increase in the number of argyrophile fibers throughout life in all the lymphoid organs studied. Eosinophilia is not correlated with aging in the lymphatic tissues of the hamster.

Age Changes in the Calcium and Magnesium Content of Rat Brain.

E. STREICHER, *Section on Aging, National Institute of Mental Health, National Institutes of Health, U. S. Public Health Service, Department of Health, Education, and Welfare, Bethesda, Maryland.*

The magnesium content of rat brain remains approximately constant from birth to 2 years of age when values are computed on the basis of wet weight, i.e., about 12-13 microequivalents/Gm. Extremely variable values for calcium were observed; in a number of instances the two halves of the same brain markedly differed from each other. In general, the same range of values for calcium was observed in all adult age groups, although there is some indication that the distribution of values in the various groups is a function of age.

The Duration of Pigmentation in the Nerve Cell Following Prolonged Administration of Acetanilid.*

N. M. SULKIN, *Department of Anatomy, Bowman Gray School of Medicine, Winston-Salem, North Carolina.*

Although pigmentation of the nerve cell is generally associated with senility, it has been observed in man at a very early age (as young as 2 years) and can be produced experimentally in young animals.

It is well known that prolonged administration of acetanilid results in anoxia in man, and it has been demonstrated in the dog and rat, administration of acetanilid results in the formation of methemoglobin from hemoglobin.

The effects of prolonged administration of acetanilid on the nerve cells of the rat was studied in 36 young animals by tubal administration of 3.7 mg./Kg. of this drug daily for periods up to 90 days. At the end of 90 days, 18 of the animals had been sacrificed and the administration of acetanilid was discontinued in the remaining 18 rats. In the group of animals which was sacrificed, 12 rats which had received acetanilid for periods of 45 days or more were characterized by the presence of lipofuscin pigment in the neurons of the autonomic and sensory ganglia, the spinal cord and portions of the brain. Normally, pigment is not observed in nerve cells of rats under 900 days of age. The remaining rats were sacrificed at intervals from 6 months to 18 months following the cessation of the administration of the drug. In these animals pigment was observed to be present in the same manner as in the first group.

It is therefore concluded that once lipofuscin pigment is formed in nerve cells it remains for the duration of the life span.

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Age as a Factor in A.C.T.H.-Induced Arteriosclerosis in the Rat.

B. C. WEXLER AND B. F. MILLER, *May Institute for Medical Research of the Jewish Hospital Association, Cincinnati, and the Department of Pathology, University of Cincinnati School of Medicine.*

Excessive activity of the human pituitary-adrenal system, as in Cushing's disease, seems to cause arteriosclerosis and premature aging. We have attempted to induce arteriosclerosis in the rat by a similar mechanism. (It should be noted that the rat has hitherto been exceptionally resistant to experimental arteriosclerosis.) To subject the animals to hyperadrenocorticalism, subcutaneous injections of A.C.T.H. were given to weanling (23-day-old) and also to 12 month-old Sprague-Dawley rats. Ten days before treatment, some had one kidney removed to condition the animal to the nephrosclerotic action of the increased circulating steroids. Injections of A.C.T.H. were given to all animals every day for 48 days. The rats ate a standard diet.

The weanling rats had no pathologic conditions. The older animals developed striking changes in their arteries. Females displayed an intense arteriosclerosis which extended from the aortic arch to the peripheral vessels; in some instances aneurysms were present. In marked contrast, the males showed no arteriosclerosis. Instead, in this sex, periarteritis nodosa and premature senile fibrosis of the testes were produced by the A.C.

T.H. injections. Unilateral nephrectomy intensified all types of pathology induced by A.C.T.H., but was not essential.

The older rats used by us were not senile animals, but mature adults. It seems that exogenous A.C.T.H. may have changed the age level at which arteriosclerosis, periarteritis nodosa, and testicular fibrosis appear. Our experiments also suggest that excesses of pituitary-adrenal activity deserve further investigation as possible mediators of the aging process.

SECTION ON CLINICAL MEDICINE

Abstracts edited by J. T. Freeman, M.D.

The Problem of Coronary Artery Disease.

C. S. Beck, *Professor of Cardiovascular Surgery, Western Reserve University, University Hospitals, Cleveland.*

When a coronary artery is occluded, the fate of the patient depends upon the amount of blood that gets into ischaemic muscle. Quantities of blood in the range of several cubic centimeters per minute make an important difference in determining what happens after an artery is occluded. Two things can happen after an artery is occluded. One of these is due to the changes in the oxygen content between ischaemic muscle and well oxygenated muscle. This checkerboard distribution of oxygen produces anginal pain, electrical instability, and currents that might be strong enough to fibrillate the heart. The other reaction produced by occlusion is death of muscle. These two reactions should be distinguished one from another because they produce different types of death and yield to different forms of treatment. Most of the fatal heart attacks are due to differences in oxygen content in the heart muscle. The total coronary inflow in most of these instances is adequate to maintain the heart beat, but because the blood is not evenly distributed throughout the heart muscle, fibrillating currents are produced and these kill. Surgical operation can bring about a more even distribution of blood which enters the heart through the diseased blood vessels. This operation does not add blood from outside sources: it distributes the blood that is there so that it can be utilized in a more effective way. The operation accomplishes this by producing intercoronary channels. These are connections between one small artery and another so that a red cell, once it enters the coronary circulation, can go anywhere within the heart's substance where it can do the most good.

The operation consists of mechanical abrasion of the lining of the parietal pericardium and the surface of the heart; the application of a mild inflammatory agent in the form of powdered asbestos to the surface of the heart; narrowing of the coronary sinus and the application of the pericardial fat to the surface of the heart. The experimental background for the operation consists of about 6,000 experimental operations on dogs' hearts over the past 25 years. The operation has sound physiologic basis and these physiologic facts are here to stay.

The results on the patients are good. Almost every patient operated upon is either completely relieved of pain or has a significant reduction of pain and is back to work. The operation has limitations, in that it does not cure the disease, but at the present time, it is the most effective treatment for coronary artery occlusion and angina pectoris. In the last 178 consecutive patients operated upon there were 2 operative mortalities. In a recent editorial, the *Lancet* of London, stated there is "a good case for giving the operation an extensive trial, and results so far offer grounds for sober optimism."

Studies of the Gastro-Intestinal Tract in the Aged.

T. Cohen, and L. Gitman, *Brooklyn Hebrew Home & Hospital for the Aged, Brooklyn.*

A study is being made of individuals 65 years of age and older in order to survey their gastro-intestinal status.

They are all carefully questioned regarding gastro-intestinal complaints, and a complete physical examination is done. Whenever possible, a gastro-intestinal and gallbladder series and barium enema are done in each patient. In addition, a chest film, electro-cardiogram, complete blood count, urinalysis, and routine blood chemistries acompany the work-up.

The study has been formulated to provide information concerning the following: 1) Evaluation of the gastro-intestinal symptomatology in these people; 2) Determination of the incidence of pathologic radiographic findings; 3) Correlation of objective and subjective findings; 4) Comparison of these results with similar findings in the general population under age 65.

The series consists of approximately 100 individuals, and several conclusions can be tentatively drawn: 1) The general impression that gastro-intestinal complaints are frequent in the aged is not confirmed. Aside from constipation there is a paucity of complaints referable to this system. 2) The amount of symptomatology does not parallel the radiographic findings, the radiographic abnormalities outnumber the gastro-intestinal complaints.

A Study of Osteoporosis in the Experimental Animal Employing Strontium 85.

L. J. Cordrey and J. H. Christie, *Departments of Orthopedic Surgery and Radiology, Highland View Hospital, and Western Reserve University, Cleveland.*

The Ca, P, and protein content of normal mice has been determined by ashing of mouse femur following autopsy and analysis using the flame photometer. A parallel study has been conducted on castrate mice of the same age. X-ray examation of these animals employing standard technique and with the use of a contrast block has been conducted simultaneously on all animals studied.

Factors regarding deposition of strontium in bone were determined. The animals were injected with 10 microcuries of Strontium 85. Counts were taken every 3 to 7 days and the amount retained compared with a standard. A total of 10,000 counts were collected. It was established that there is a definite biologic turnover of Strontium 85 in the mouse and that this is triphasic.

The experimental animals were sacrificed, autopsies were performed, and various organ samples were collected. To evaluate the effect of age in bone deposition of Strontium 85, mice 2½ months old and mice more than 4½ months old were subjected to similar experimentation. The results indicated that the younger the animals the longer the biologic half-time.

A group of castrate mice older than 4½ months were injected with Strontium 85 and counted as described above. Results showed a significant alteration in the excretion of Strontium but no alteration in pattern of excretion.

It is quite apparent from these data that age plays a significant part in the degree of deposition of Strontium 85 in bone.

Arthritis, Arthrosis, and Arthralgia in the Elderly.

L. W. CROMWELL, *Scripps Memorial Hospital, La Jolla, and San Diego County Hospital, San Diego.*

(Abstract not received.)

Atomic Medicine in Geriatrics.

L. E. FARR, *Medical Director, Brookhaven National Laboratory, Upton, Long Island, New York.*

Most diseases of maturity are characterized by changes in function or structure which arise either without outside stimulus or after such a long period of time that the provoking agent cannot be identified. These diseases have been loosely characterized as degenerative. With age there is a constantly shifting pattern of function described as growth development and senescence which is independent of any disease and is inherent in life itself. For separation of these two processes and in particular for study of degenerative disease processes the products, machines and concept of nuclear physics provide the physician with powerful tools which ultimately will result in better control over undesirable states. Activation analysis, neutron capture therapy, and tracer applications with long and short lived isotopes permit a range of study both anatomical and structural. Examples of these applications will be discussed and their significance for medicine relative to older persons will be pointed out.

A New Approach to the Clinical Classification of Senility.

O. L. FRIEDMAN, AND L. O. FRIEDMAN, *Holbrook Manor, Inc., Holbrook, Long Island, New York.*

Due to the increasing interest in the field of geriatrics in general—a result of the increasing world population of elderly people—this paper attempts to explore one of the more prominent geriatric problems, senility, from the anatomic, pathologic, and psychiatric points of view.

A brief discussion is included in connection with presenile dementia, Alzhemer's and Pick's disease, and cerebral arteriosclerosis with psychosis in relation to senile dementia in the above-named spheres of experimental and clinical investigation. The changes in the senile brain, cellular and vascular alterations, changes in the cortical neurons, selection of cell degeneration, and neuropathologic and clinical studies by the author and by several research workers and gerontologists such as Cowdry, Stieglitz, Nielson, Thompson, Thewlis and others, are focused upon in this paper. The treatment of senility in mental institutions and nursing homes specially designed for the senile patient is outlined briefly, as is the role of the newer drugs, both from the experience of the authors and of several recognized authorities.

It is believed that this paper presents an original point of view on the subject, in regard to the attitudes, diagnosis, and treatment of what is becoming an ever-increasing sociologic, economic, and medical problem, that there is such an entity as the happy senile patient, a result of simple and gradual deterioration, with and without cerebral arteriosclerosis, without frank psychotic manifestations, who is being lost in the larger classification of senility, and who requires a fresh approach on the part of the medical profession.

Nutrition, Life Tenure, and the Incidence of Degenerative Diseases.

J. I. GOODMAN, *Heights Medical Center Building, Cleveland Heights.*

The two major nutritional disturbances found among the chronically ill as well as among the so-called normal population are malnutrition on one hand and obesity on the other. This is a study of caloric intake measured by weight gain or loss in each patient with an evaluation of the methods of procedure, the use or nonuse of supplementary medication, and the changes in body function. The many causes of undernutrition and the development of dietary inadequacy have been sought and are discussed as well as the clinical findings in obesity. Here, too, emotional instability is frequent, and as these patients return to a more normal weight there is a return to more normal activity and better physical health. This discussion is based on a study of the chronically ill patients at the Cuyahoga County Nursing Home in Cleveland.

Tolbutamide in the Management of the Elderly Diabetic.

G. J. HAMWI, *Associate Professor of Medicine; Chief, Division of Endocrinology and Metabolism, Ohio State University, Columbus.*

The experiences obtained in treating approximately 150 patients with Tolbutamide will be presented. In general, this compound proved to be most effective in the older, milder diabetic. Since the diabetes in the older diabetic is usually mild, it follows that this oral hypoglycemic agent is most useful in the geriatric group of patients.

The obvious advantages of this compound are: 1) Its hypoglycemic activity; 2) Tolbutamide is a sulfonamide derivate. The undesirable side reactions of sulfonamides have been observed since 1935; 3) The relative paucity of severe hypoglycemic reactions; 4) The relatively slight toxicity that has been reported to date; 5) The convenience offered to the patient in an oral preparation.

The disadvantages are: 1) The lack of ability to predict the effectiveness of these compounds in any one patient; 2) The lack of effectiveness of this compound in the presence of acidosis or severe stress of any sort; 3) The possibility of minimizing the importance of dietary control by substituting therapy with Tolbutamide; 4) The theoretical possibility that the lowering

of the blood sugar by itself may be inadequate to prevent other associated metabolic derangements; 5) The unknown potential effect of this compound on the control or production of chronic degenerative vascular complications.

The Outlook of Vascular Surgery Upon the Aged.

C. Hitchcock, and T. O. Murphy, *Department of Surgery, University of Minnesota, Minneapolis.*

Over the past decade the rapid advances of vascular surgery, and especially those techniques of arterial replacement, have caused us to make marked changes in our approach to the manifestations of arteriosclerosis in the aged. The results of surgical repair of aneurysms and occlusive vascular disease have been very encouraging and further, these techniques may be employed with a minimum of risk to the patient. Arterial replacement in the extremities may be easily carried out even under local anaesthesia.

This presentation will discuss the results of various types of arterial replacements in over 160 aneurysms and a total of over 250 arterial grafts. Some of the newer techniques of attempts at cerebral revascularization in instances of internal carotid artery thrombosis will also be presented.

The Effect of Paget's Disease upon the Cardiovascular System.

H. N. Hultgren and E. Caul, *Department of Medicine, Stanford University School of Medicine, Stanford, California.*

Paget's disease has been alleged to involve the cardiovascular system by: 1) An increased incidence of calcific valvular disease; 2) An increased cardiac output; 3) An excessive degree of arteriosclerosis. Observations supporting these contentions, however, are scanty. For these reasons a clinical study has been made of 121 patients with severe, generalized Paget's disease, and 417 control patients in a similar age group who were not affected by the disease. Autopsy findings in 27 patients were compared with similar data from 2 control groups: a series of 201 patients in the same age group and 50 unselected patients who were all over 80 years of age.

The following observations were made: 1) Grossly visible calcification of the mitral and aortic valves was present in 59 per cent of 27 autopsied cases of severe Paget's disease compared to an incidence of 18 per cent in 201 control cases in the same age group and 40 per cent in the group of patients over 80. The incidence of significant calcific aortic stenosis in the 3 groups was 31 per cent, 7.5 per cent, and 10 per cent, respectively; 2) Clinically evident aortic stenosis was present in 21 per cent of 66 patients with severe Paget's disease whose clinical records were reviewed compared to an incidence of 4 per cent in 417 control patients; 3) An analysis of blood pressure, pulse rates, calculated cardiac outputs (Starr formula), and heart weights from patients with severe Paget's disease revealed no deviation from similar data obtained from control subjects; 4) Clinical manifestations of arteriosclerosis such as cerebrovascular accidents, angina pectoris, or myocardial infarction were no more frequent in patients with Paget's disease than in control patients. The incidence of coronary and aortic arteriosclerosis was similar in the 2 groups. It is therefore concluded that the principal effect of severe Paget's disease upon the cardiovascular system is the development of an increased incidence of calcific valvular disease involving both mitral and aortic valves resulting in a striking increase in the incidence of clinically significant aortic stenosis. In addition, these data provide further support to the concept that aortic stenosis in the elderly may be of non-rheumatic origin.

Nutritional Consideration of the Older Person.

W. B. Kountz, *Division of Gerontology, Washington University School of Medicine, St. Louis, Missouri.*

Too much emphasis, in my opinion, has been placed on the diet without considering the fact that the older person does not have the ability to utilize food. We are dealing with an individual who is metabolically different from a child or a person in middle age, as a general rule. Some few retain the quality of being able to burn and utilize food substances properly. It has been established that most individuals of older age have difficulties of the sugar burning mechanism as revealed by glucose tolerance curves, in comparison to those of a younger age. The percentage of normal curves in people past 60 is relatively small and of the seven different types of curves that occur in man, the curves indicate a much lower efficiency in burning carbohydrate. In other words, they approach either the mild diabetic or diabetic picture.

Likewise we find that utilization of protein may become a problem in the average older person who has not been treated. First he tends to digest and absorb it, then when he gets it into his body he may fail even to utilize it. In addition to the disturbances of utilization, there seems to be an increase in mobilization with the utilization, which tends to result in a loss of the normal protein content of the body. These individuals are frequently thrown into a negative state of nitrogen balance by the simplest forms of stress. The administration of hormone substances will tend to prevent the occurrence of protein loss.

Likewise the process of fat utilization seems to be interfered with, as revealed by the electrophoretic pattern. The beta-lipoprotein is generally increased in older people and seems to be a typical manifestation.

This picture may be modified with proper diet and hormone administration. A discussion of the low values of vitamins, particularly A, C, and D, may be noted. These substances are generally low, as are many of the trace minerals. Supplementary intake is important.

Psychiatric Observations in an Old Peoples Home.

V. A. Kral, *Gerontologic Unit, Allan Memorial Institute of Psychiatry, McGill University, Montreal.*

The population of the Hebrew Old Peoples Home in Montreal (71 men and 91 women) was examined psychiatrically, neurologically, and psychologically. The age of the subjects ranged from 60 - 96 years, with a mean of 79.3 years.

Five groups could be distinguished on the basis of the psychiatric examination. Group A (37 cases): well

preserved personality, preserved judgment, appropriate emotional reactions, no memory loss. Group B (30 cases): well preserved like Group A but with mild memory loss involving occasional difficulties in recalling names or dates which were available at other times. No loss of recent memory, no difficulties in orientation. Group C (24 cases): preserved memory but signs of functional psychoses of the affective or paraphrenic type. Group D (49 cases): memory loss with the characteristics of an amnestic syndrome (loss of recent memory, difficulties in orientation and tendency to confabulations). Group E (22 cases): memory loss like in Group D plus psychotic signs of an affective or delusional nature. These findings are discussed and compared with the psychiatric nosologic entities of mental disorders in senescence.

On phenomenologic analysis 2 different types of senescent memory impairment could be distinguished: One, as found in Group B, consisted mainly in difficulties in recall and resembled nominal aphasia, the other as found in Groups D and E, seemed related to difficulties in registration and represented the senile amnestic syndrome proper. On statistical analysis both types of memory impairment were positively related to increasing age. The senile amnestic syndrome, however, was significantly more frequent in women than in men. There was no significant relationship between memory loss of either type and the presence or absence of functional psychotic signs, cerebrovascular disease, hypertension, or diabetes. The implications of these findings both for geriatric medicine and psychiatry are discussed.

An Affirmative Approach to Clinical Education in Geriatrics.

C. D. LEAKE, *Ohio State University, Columbus.*

Humanity is rapidly approaching a biologic crisis for which it is not prepared. This is the explosive population increase which is occurring all over the world as a result of the practical success of the general health effort of the past half-century. The most significant feature of the present population explosion is the huge increase in the number of old people which is threatening the stability of cultural patterns everywhere.

For the first time in its history, mankind is confronted with a huge and growing number of old folks, who pose frightening problems in economics, politics, human relations, housing, and care. They are not prepared adequately to take care of themselves, and the rest of the people are not prepared to take care of them, either.

In order to assess factors influencing aging, there must be a broadly developed scientific program of research into such factors. This will require interdisciplinary cooperation. Basic biologic problems of senescence must be correlated with factors influencing the aging process in people. Many of the factors associated with aging are psychologic and sociologic. These call for careful analysis with the development of systematic programs for training people for old age. Such training might well begin in adolescence and in young adult life, when the initiation of the biologic process of aging really begins.

Thyroid Patterns, Their Identification and Management After Age Sixty-Five.

T. H. MCGAVACK, AND WINNIFRED SEEGERS, *New York Medical College, New York.*

A study has been made of the thyroid and its function in more than 600 patients in a chronic disease hospital and home. The subjects ranged in age from 44 to 99 with between 90 and 95 per cent over the age of 60; 20 and 25 per cent over the age of 80. Approximately equal numbers of the two sexes are included. Various clinical and laboratory parameters of thyroid function have been oriented in relation to the physical characteristics of the thyroid gland. Of the women surveyed, approximately $\frac{1}{8}$ showed normal glands; less than 3 per cent diffusely enlarged thyroids; from 3 to 5 per cent showed enlarged nodular organs; in about $\frac{1}{4}$ the gland was small; in a little less than $\frac{1}{5}$, one lobe only was palpable and in between 35 to 40 per cent, the gland was not palpable at all. One striking difference was seen in examining the men, namely, that in nearly $\frac{2}{3}$ of them, the gland was not palpable. The uptake of I^{131} by the thyroid varied from 3 to 40 per cent with an over-all average of 20.0 per cent (men) and of 20.4 per cent (women) of those patients over 60 years of age. The serum protein bound iodine values varied from 2.4 to 9.1 micrograms per 100 cc., with an over-all average of 6.17 micrograms per 100 cc. In none of the cases were there overt signs of hyperthyroidism or hypothyroidism. In so far as basal metabolic rates could be established and extrapolated with existing tables, they were within normal range for each subject. Values for serum cholesterol varied quite widely but bore no apparent relationship either to the physical status of the thyroid or to the general condition of the patient. While some of the signs commonly associated with myxedema may be seen in older people, it was not possible to correlate these directly with the above parameters of thyroid function. A definite relationship seems to exist between thyroid and pelvic disturbances. The percentage of this correlation will be compared with a relationship of thyroid disease to some nonspecific non-related condition.

The functional responsiveness of the thyroid was tested in a limited number of patients by TSH administration. Such responses can be considered normal.

The Mechanisms of a Geriatric Clinic and Its Place in the Community.

R. T. MONROE, *Director, Division of Health and Personality Equilibrium, and Vice President, The Age Center of New England; Consultant, Pearl Memorial Clinic, Peter Bent Brigham Hospital; Associate in Medicine, Peter Bent Brigham Hospital and Harvard Medical School, Boston.*

Sixteen years' experience with a geriatric clinic in the Peter Bent Brigham Hospital, Boston forms the basis of considerations of what can and what cannot be expected of it. The important variables are the community, the old people in the community, the nature of the facility in which the clinic is housed, its leadership and its relationship with other medical and paramedical facilities.

Relation of Blood Pressure to the Electroencephalogram in People Over Sixty.

W. D. Obrist and R. H. Dovenmuehle, *Duke University School of Medicine, Durham, North Carolina.*

A statistical analysis is presented of the relation between blood pressure and EEG as obtained on a total of 220 elderly subjects in 3 independent studies: 1) 103 hospitalized psychiatric patients in Connecticut, 2) 57 similar patients in North Carolina, and 3) 60 mentally healthy people at a home for the aged in Florida.

The results indicate that aged psychiatric patients with mild to moderate elevations in blood pressure (150-200 systolic and 90-110 diastolic) have a higher incidence of normal electroencephalograms than those with low or average pressures. The latter tend to have abnormally slow EEGs, particularly diffuse slowing. EEG differences between blood pressure categories were most pronounced in cases with clinical evidence of cardiovascular disease. These findings were statistically reliable in both groups of psychiatric patients, suggesting that an elevated blood pressure may serve to maintain normal electrocortical activity. Similar trends were observed for the small group of mentally healthy old people, although they lacked statistical significance. Data on a larger series of 130 community volunteers are now being analyzed and will also be reported.

Contractures in the Hemiplegic Patient.

M. Peszczynski, *Associate Professor of Clinical Medicine and Rehabilitation, Department of Medicine, School of Medicine, Western Reserve University; Chief, Department of Physical Medicine and Rehabilitation, Highland View Hospital, Cleveland.*

The author discusses the present lack of exact knowledge as to what a contracture is. The proportionate role of positioning (gravity), spasticity, withdrawal reflexes, and disorders of the patient's own body concept in every major contracture on the hemiplegic side is evaluated. Some current concepts of prevention of contractures in the hemiplegic patient are critically analyzed. The effect of lower extremity contractures on the hemiplegic patient's ability to learn to walk is discussed in detail.

Functional Capacities of Older Individuals.

E. Simonson, *Laboratory of Physiological Hygiene University of Minnesota, Minneapolis.*

The slope of decline of capacity for physical work with age is steepest in types of endurance performance in hard aerobic and anaerobic work, and less pronounced in types of moderate aerobic work. Although the older worker is able to maintain a satisfactory work performance in moderate physical work over several hours, there is evidence that he is working closer to the limit of his reserve capacity and needs longer recovery periods. A comparison of the effect of age and of cardiovascular disease on various types of work performance shows a great similarity in the profile of interference. It is concluded that deterioration of the cardiovascular functions plays a dominant role in the decline of work capacity with age. The work capacity of different age groups and of patients, however, shows great overlap. Cardiovascular age trends are illustrated in the electrocardiogram (conventional scalar leads, vectorcardiogram, response to exercise), peripheral circulation (photoplethysmogram), cerebral circulation (Schmidt and Kety's method), and orthostatic carotid sinus reflex (extracranial impedance plethysmogram). Evidence is presented (electrocardiogram, aortic pulse transmission time) that arteriosclerotic degeneration and age trends are concordant, and the hypothesis is advanced that arteriosclerotic degeneration may be, at least in the American population, an extreme of normal age trends. Since training and age effects on physical performance are opposite in direction, the possible counteraction to aging and development of cardiovascular degeneration by training is discussed.

In regard to the maintenance of working capacity with age, the shift from the involvement of muscular and cardio-vascular to nervous functions in the trend of industrial development must be considered. Visual performance has become increasingly important, and the age trend of several visual functions is discussed in this respect.

Serial Physical and Physiologic Tests as Criteria for Evaluation of Therapeutic Methods

G. D. Williams, *Veterans Administration Center, Martinsburg, West Virginia.*

Physical medicine and rehabilitation is a medical specialty frequently concerned with the therapy of elderly patients. The medical and other problems of older people are multifaceted, necessitating in many cases the medical "team" approach. When team therapy promises optimal results, the physiatrist is accustomed to work as a team member.

Diagnosis and treatment according to the methods of physical medicine and rehabilitation are here described. The physiatric contributions now available and under development are discussed in relation to those of other specialties.

One technique of physiatric practice, routinely used in physical medicine but generally unknown or neglected by practitioners at large, is that of serial testing of gross physical and physiologic status of patients. The technique of testing is simple; it may be done by a physician or his physiatrically trained assistant; its significance is easily comprehensible to any well trained practitioner. It is a basic technique for measuring certain aspects of efficacy of various therapeutic regimens employed in the care of the elderly patient. Examples of testing techniques are illustrated and discussed.

SECTION ON PSYCHOLOGICAL AND SOCIAL SCIENCES

Abstracts edited by Wilma T. Donahue, Ph.D.

Modulation of Speed of Response with Age.

J. Botwinick, J. F. Brinley, J. S. Robbin, *Section on Aging, Laboratory of Psychology, National Institute of Mental Health, National Institute of Health, Public Health Service, U. S. Department of Health, Education and Welfare, Bethesda, Maryland.*

The purpose of this study was to determine whether younger adults could be as slow or slower than older adults when the situation required it. It is already known that older adults are not as fast as younger ones, and increased motivation does not alter the picture. Evidence is also available that older adults have a more constant work rate over-time with continuous performance than younger adults. If it is found that younger adults can respond more slowly than older adults when the task requires it, a more complete picture of age differences in capacity to modulate speed of response will be available.

Subjects for this study were 29 men, aged 65-81 years, median= 72 years, and 23 men, aged 18-31 years, median= 22 years. All subjects were volunteers, in apparent good health and without known neurologic disease.

Results indicate that when the task requires slowness, younger adults are slower than older adults. This finding plus the evidence already available suggests that older persons operate within narrower limits of response rates than do younger persons. This limited modulation may have protective or safety effects related to adaptation.

Personal and Social Adjustment of Rural Older Persons.

J. H. Britton and W. G. Mather, *The Pennsylvania State University, University Park, Pennsylvania.*

Problem: To provide understanding of the personal and social adjustment of older persons living in a rural community. Operationally, to discover 1) the community's expectations for older persons, 2) significant variables in their adjustment, and 3) to evaluate some methods of assessing their personal and social adequacy.

Subjects: 1) Extensive study of community: In a rural Pennsylvania community of 2,000 persons, an adult member of each household (N = 487); 2) Intensive study of individuals: All persons 65 or over in the community (N = 208), 145 of whom were able and willing to be interviewed.

Procedure: Interviews were held with an adult of each household, thus locating older persons for intensive study and providing data on behavioral expectations for older persons. Then with each older subject interviews were held concerning his health, activities, and beliefs; assessments of his adjustment were made through the use of a standardized attitude inventory, items concerning personal-social relations, ratings of interviews, and projective techniques. For a selected sample of subjects, assessments were cross-validated with evaluations by a panel of community members who rated these subjects on some measures of social adjustment in the community.

Results and Conclusions: Analyses showing relationships among adjustment criteria and some social and psychologic variables significant in the adjustment of older persons in this rural community are presented and interpreted; some conclusions are drawn about the methodology of measuring adjustment of older persons.

Attitudes to Aging and Retirement of Employees in Industries by Different Economic Levels.

E. W. Burgess, *Consultant in Studies of Aging and Retirement, Industrial Relations, University of Chicago.*

A Retirement Planning Inventory consisting of 100 statements on attitudes to aging and retirement has been filled out by employees of companies in and around Chicago. The replies of the respondents have been classified by the following occupational levels: managerial, supervisory, technical and professional, skilled, semiskilled and unskilled. The findings indicate that there are considerable differences in attitudes to aging and preparation for retirement between these different occupational groups when they are analyzed by major categories of replies and by individual items.

Attitudes of Nursing Home Operators Toward Their Profession.

E. Friedman, D. Olmsted, and Anita Flint.

(Abstract not received.)

Interaction Patterns in Age.

Elaine Cumming and Lois Dean, *University of Chicago.*

An aging paradigm based upon amount and type of interactions has been developed in the Kansas City Study of Adult Life. A formulation emphasizing the symmetry between adolescence and old age is offered, and a typology of success and failure in age is developed and illustrated with case material from our panel of adults.

Illustrative data are offered in support of the proposition that middle-aged people and old people radically differ from each other in the amount of engagement they have with life; middle-aged people being fully engaged and older people, like adolescents, somewhat disengaged. Evidence is presented that this relative disengagement of age is more functional than malfunctional and that success and failure in aging depends not upon attempting to halt the disengagement process but rather in maximizing its rewards and minimizing its deprivations.

The Significance and Content of Leisure Activities from Age Forty to Seventy.

R. J. Havighurst, *University of Chicago.*

Most of the research on the leisure activities of people has been aimed at learning about the content of these activities. There have been a number of studies of what people do in their leisure time and how much time they spend in these activities. On the other hand, the significance of leisure to people has been relatively neglected.

The purpose of this study was to explore the interrelations of two ways of analyzing leisure activities—content and significance—and to find out how these are related to age, sex, social class, and personality characteristics.

Significance was a general term applied to a set of 19 variables such as: autonomy, creativity, instrumental vs. expressive, relation to work, relaxation, expansion of interests.

Significance of leisure activity was measured by a set of rating scales applied to the two favorite leisure activities of each of a sample of 234 people aged 40-70 who were interviewed in the Kansas City Study of Adult Life. The study was aimed at answering the following questions: 1) Does the significance of leisure activities vary with age, sex, and social class? 2) Does the significance of leisure activities vary with personal adjustment? 3) Does the significance of leisure activities vary with the content of these activities?

It was found that: 1) There is remarkably little change of significance of leisure activities with age (between 40 and 70); 2) The significance of leisure activities is more closely related to personality than to age, sex, or social class. Thus, leisure activity is an aspect of personality; 3) Several different leisure activities can have the same significance to people; therefore people of different age, sex, and social class can derive similar values from their leisure, even though the content of their leisure activities is different.

Preparation for Retirement of Hourly Wage Employees.

W. W. HUNTER, *University of Michigan.*

A preparation for retirement program was offered to a group of hourly wage employees 60 years of age and over from three industries. Data were systematically collected and tests of significance applied to them in order to answer the question of whether or not participation in the program resulted in significant changes in the number of participants who acquired information, made plans for retirement, and put their plans into action.

Attitudes Toward Illness in the Aged.

R. L. KAHN AND A. I. GOLDFARB, *Department of Neurology and Psychiatry, Home for the Aged and Infirm Hebrews of New York, New York.*

Problem: Recent studies have demonstrated that institutionalized aged persons have fewer somatic complaints (Tuckman et al) and are more inclined to overvalue their physical condition (Shrut) than non-institutionalized persons. The purpose of the present study was to determine some of the relevant factors associated with attitude toward illness in the aged.

Population: Fifty persons residing in a home for aged. Half were selected at random from current psychiatric referrals; the remaining 25 were sampled from the balance of the residents.

Method: 1) A standardized series of questions testing orientation and attitude toward illness. The two questions for this latter aspect were: "What is your main trouble?" and "If you had one wish, what would you wish for?" Each patient was classed depending on whether none, 1 or 2 of his responses to these questions referred to physical illness; 2) The Face-Hand test (Bende et al); 3) A perceptual task in which the subject had to find a series of simple geometric figures embedded in a complex background; 4) The medical condition of each patient was rated using a modification of Zeman's functional classification system.

Results and Conclusions: 1) The number of somatic responses is highly correlated with the number of errors made in perceiving embedded figures. It is unrelated to age, sex, orientation, response on the Face-Hand test, or to psychiatric or medical status; 2) Absence of somatic response is related to 2 different kinds of factors, a) a capacity for active interpersonal relatedness, and b) the presence of denial tendencies.

The Role, Status, and Participation of the Aged in a Small Community.

J. S. MCCRARY, *University of Chattanooga.*

(Abstract not received.)

The Attitudes of Middle-Aged Persons Toward Growing Older.

BERNICE L. NEUGARTEN AND D. C. GARRON, *University of Chicago.*

This report is based on interview data obtained from a sample of 600 men and women aged 40 to 70 residing in a midwestern metropolitan area. The interviews dealt with the respondent's evaluation of his life in the present as well as his expectations and feelings about growing older.

Findings are reported concerning the patterns of relationship that exist between evaluations of the present and attitudes toward the future and concerning how positive and negative attitudes vary according to sex, age, social class, marital status, and occupational status of respondents. Finally, these findings are related to the findings from similar studies based on samples of old people.

Cultural and Environmental Factors Affecting Complex Perception in the Institutionalized Aged.

M. POLLACK, R. L. KAHN, AND A. I. GOLDFARB, *State of New York Department of Mental Hygiene, Queens Village.*

Problem: Defects in complex perception have been reported as increasing in frequency with age (cf. Green and Bender). These changes have been attributed to the process of aging per se. Marked individual differences have been noted, however, between individuals in the same age group and between individuals in different institutions. This study is an investigation of some of the cultural and environmental factors associated with these differences.

Population: 325 subjects over the age of 65 were randomly selected from a variety of nursing homes and homes for the aged.

Method: 1) Each subject was tested for perception of simultaneous touches to face and hand (M. B. Bender's Face-Hand Test, 10 trials with eyes closed and 10 with eyes open); 2) A mental status examination of 10 items was administered. The number of errors served as the index of impairment.

Results: 1) While this population as a group made significantly more perceptional errors than do persons under 65, the correlation with age per se within the group is low; 2) Impaired perception was highly correlated with errors in mental status, extent of physical mobility, educational and occupational background, and the character of the institution in which the subject resides; 3) The number of errors made with eyes open was almost as great as with eyes closed; 4) Errors were most commonly made for the hand, confirming the pattern previously described.

Conclusions: Alterations in complex perception cannot be ascribed to aging as a physiologic decline unrelated to socio-psychologic factors. The cultural background of the individual and the immediate socio-psychologic situation influence complex perception.

Jobs at Eighty.

S. L. Pressey, *Ohio State University, Columbus.*

As a result of a continuing search for and study of superior old people, a substantial number have been found who are continuing some form of remunerative work even into the nineties. The present report deals with individuals who have thus continued economically productive well past the usual time of retirement. It concerns both their traits and the types of work they did.

As might be presumed, these persons were superior in health and ability and of vigorous personality. They were doing most commonly professional or managerial types of work, but some handicapped cases were included, and a range of work was represented.

It is concluded that (a) Many old people have vocational potentialities, (b) Types of work suitable for them should be recognized, and (c) Tapering or shift-down in responsibility and status should become as accepted a feature of the older years as are gains in these respects in young adulthood.

Interviewers' Attitudes in a Nationwide Study of Older People.

Ethel Shanas and Selma F. Monsky, *University of Chicago.*

In a nationwide survey of the health needs of persons 60 years of age or more, conducted by the National Opinion Research Center under the auspices of the Health Information Foundation, 2000 older persons were interviewed, using a staff of two hundred interviewers.

No study can be better than its basic data, and therefore, special attention has been given to the effects of the interviewer in this research. Only a few problems related to interviewing will be considered in this paper. These include: (1) Enlisting the cooperation of the older respondent; (2) Comparability of older respondents with other segments of the population in terms of availability and cooperativeness; (3) Success of interviewers related to their attitudes toward the aged at the beginning of the study; and (4) The effect of this study on interviewers' attitudes toward the aged.

Psychologic Factors Associated with Differential Patterns of Institutional Versus Community Living Arrangements in a Geriatric Group.

J. W. Stafford and Claire M. Vernier, *Catholic University of America and Veterans Administration Hospital, Baltimore.*

One aspect of the general geriatric problem is that of the extent to which psychologic factors, independent of physical disabilities, influence an older individual's choice of living arrangements. Because of its Domiciliary program for veterans chronically disabled and unable to earn a living, the Veterans Administration has been directly concerned with many phases of an institutional care program.

In 1951, an inter-disciplinary research project was initiated at the Martinsburg, West Virginia VA Center. The research program included a medical-social-psychologic assessment of three different samples: 1) Members in the Domiciliary at one time, regardless of length of stay; 2) New admissions; 3) A matched group of veterans equally physically disabled and eligible for Domiciliary care, who chose to remain in the community.

Four kinds of living patterns can be identified: 1) Permanent domiciliary residents, members who are admitted once and remain indefinitely; 2) Intermittent domiciliary residents, members who have repeated admissions and discharges; 3) One-time, short-term domiciliary residents, individuals who are admitted only once and leave within 6 months to return to the community indefinitely; 4) Community residents, who although physically disabled and eligible for domiciliary care, never seek admission.

Twenty-five cases were selected for each of these 4 patterns of living. The groups were matched for age, race, intellectual level, socio-economic status, and degree and kinds of physical disability.

Scores, selected from a completed factor analysis of 4 projective psychologic tests, were tabulated and statistical reliability of differences determined.

Results indicate that certain psychologic factors are critically important in the differential living patterns chosen by older, physically disabled individuals.

Retirement and Health.

W. E. Thompson and G. F. Streib, *Cornell University, Ithaca, New York.*

This paper reports the findings of the Cornell Study of Occupational Retirement concerning the relationship between retirement and health. Our study, like many others, shows a disproportionate amount of poor health among retirees, but the nature of the relationship is obscure. Does it reflect a high incidence of retirement among those in poor health? Or does retirement, with its attendant change in routine and relative inactivity, lead to a deterioration of those who retire? The longitudinal design of the Cornell Study makes possible an analysis of these alternative hypotheses.

The present analysis includes 2000 persons, all of whom were employed when first contacted in 1952-1953. By 1954-1955, 588 had retired. By 1956, an additional 372 had retired. Data were gathered by means of self-administered questionnaires and, for a sub-sample, by medical examinations usually performed by company physicians. Thus health not only

is evaluated by the individual himself but also is objectively evaluated by an examining physician.

Without exception, our findings show that voluntary retirement follows from poor health. Those who hold an unfavorable attitude toward retirement tend to change their mind when their health becomes poor, and they also tend to change their working status as a result of changes in health, regardless of their attitude toward retirement. Our findings do not in any case support the hypothesis that retirement has a deleterious effect on health. In fact, our medical examinations suggest that retirement leads to a differential improvement in health. While, over-all, health remains a serious problem for some older people, we conclude from our findings that it must be understoood in proper perspective and that it is not a condition which follows from voluntary or administrative retirement.

The Projection of Personal Symptom into Stereotype about Aging.

J. TUCKMAN, AND I. LORGE, *Division of Mental Health, Department of Public Health, Philadelphia, and Teachers College, Columbia University, New York.*

The purpose of this study is to estimate the relationship between physical and psychologic changes, reported by the individuals as either bodily, or as mood and feeling symptoms and the number of stereotypes he accepts about old people and the older worker. The hypothesis to be tested suggests that the greater the number of symptoms an individual has the greater the number of stereotypes he accepts.

Reports of bodily and of mood and feeling symptoms were obtained through the use of the Cornell Medical Index, a self-administered paper-and-pencil inventory of 195 questions requiring a "yes" or "no" response. Acceptance of stereotypes about aging was obtained by two questionnaires also requiring a "yes" or "no" response to specific statements (of which most are not supported by research evidence) about old people and the older worker.

The relation between symptom and stereotype was studied in two samples: a younger group of 394 graduate students and an older group of 87 institutionalized and noninstitutionalized adults.

Despite the possibility that response set may account for the relation between symptoms and stereotypes, the evidence does indicate acceptance of stereotypes as a function of reported symptoms. The tendency for those who have the disability to believe that it is generally true of the class of old people and older workers is operating against response set and against the tendency of people to accept stereotypes about aging in general.

An Orientating Study of the Memory of Old People.

R. J. VAN ZONNEVELD, *Coordinating Physician for Gerontological Research, National Health Research Council, T. V. O., The Hague, Holland.*

A socio-medical survey among 3000 aged people in a Dutch town included among other things a simple memory test. This test consisted of a number of questions from the Wechsler Memory Scale, which were partly modified for the purpose. The questions had reference to orientation, knowledge obtained in the early school-years, auditive and visual memory. The cooperation of the aged was good, only some percent refused to answer all memory-questions. As could be expected, a decreasing well-functioning of the memory was found with increasing age. Though the test was relatively very simple, a significant difference between the scores of the higher and lower social classes could be demonstrated.

The nature of the test, the data on several comparisons as well as the results of separate questions will be described.

Variations in Marital Status of the Older Population of the United States According to Residence and Region.

I. L. WEBBER, *Institute of Gerontology and Department of Sociology and Anthropology, University of Florida, Gainesville.*

Although numerous studies of the numbers, distribution, and characteristics of the older population of the United States have been reported, little or no attention has been directed to variations which occur among residential areas and regions. The purpose of this paper is to examine such variations in one characteristic, marital status.

Official census data on the population aged 65 and over as of April 1, 1950, are employed. Marital status is categorized as single, married (husband or wife present or absent), widowed, and divorced. The analysis is made on the basis of urban, rural-nonfarm, and rural-farm residence; regional residence; race; and sex.

Older single men were found in highest proportions in rural-nonfarm areas, single women in urban areas; married men and women occurred in largest proportions in rural-farm areas; widowed men and women were most in evidence in urban areas; and divorced men were most important proportionately in urban and rural-nonfarm areas, divorced women in urban areas.

The Northeast had considerably more than its pro-rata share of single men and women and of widowers. Somewhat more than the expected share of single men, married women, and divorced men lived in the North Central Region. The South had more than its proportionate share of married men and widowers. A disproportionately large share of single men and more than twice the pro-rata share of divorced men and women resided in the West.

SECTION ON SOCIAL WELFARE

Abstracts edited by Florence E. Vickery

A Golden Age Center—An Experiment in Public and Private Agency Cooperation.

LUCIA BING, *Staff Member, Golden Age Center of Cleveland.*

The Cleveland public housing authority has allotted the ground floor rooms of its two-year-old 14 story building to a Red Feather agency as an activity center for older people. A staff of 5, assisted by excellent volunteer service, directs classes in handcrafts, public speaking, choral singing, drama, and poetry. The senior citizens elect their own club officers, publish a newspaper, run a cafeteria, entertain Golden Age Clubs and run their own movie projector. Summer travel trips are popular. Medical and nursing services must be supplied by community agencies and are in short supply.

Group Work in Homes for Aged.

NELIDA A. FERRARI, *Group Worker, Benjamin Rose Institute, Cleveland.*

This presentation concerns observations and findings related to a period of two years of group work practiced in homes for the aged. It is a part of a three-year study-project planned originally for three Homes in Cleveland. The paper refers to the work in one of these homes where the average age of the residents is 81.5. The first part consists of an analysis of the setting as one which differs from regular settings, pointing some of the ways in which it affects the residents of the home. Many paradoxes are observed in this setting where individuals are living in a group but still are lonesome. They are alone but they do not have privacy.

The approach used by the worker in facing problems of motivations is described as well as some of the first steps taken in the initial development of the program. The criteria for a program which is serving people living in a "group," must be individual ones. Here the individualization of needs is emphasized as well as the type of reactions of residents toward their peer group. Some particular illustrations are given in the presentation of the evaluation of the social group. This covers the program during the first two years and the reactions of residents to it, including details concerning changes in the behavior of residents. This part also includes the effect of the program in the total life of the home and the residents relationship with the community. A displacement of interest is observed when the Home changed from a self-centered organism to one connected with the neighborhood and the city.

The last part of the paper deals with the need for more knowledge related to older persons in order to develop techniques which can be used to communicate with them. Insufficient or deficient communications with older persons is one of the reasons for our lack of success in some cases. Our own attitudes toward older persons are factors affecting work with them. New tools and methods need to be developed.

Nutrition and Special Diets in Homes for Aged.

J. G. GOLD, *Executive Director,* M. DRAY, *Assistant Executive Director, Orthodox Jewish Home for the Aged (BMZ), Chicago.*

Presentation of the ever-present problems of serving meals on a mass feeding basis is the subject of this paper. While the approach to issues and methods for solving them are presented, the intent is to establish that the variety of solutions is influenced by the individuals involved.

When the homes were simply domiciliary units, small pretense was made at a dietary effort. However, with increasing emphasis on medical aspects, nourishment and special diets have become matters of vital interest.

Feeding is a three-times daily point of contact between staff and resident. The relatives also frequently are concerned with food or situations precipitated about food or its service.

Training the staff and working to get the residents involved are of great value. Understanding and the opportunity to cooperate in a mutual venture are practical means toward minimizing as well as solving problems.

The difficult patient should not be coerced, but at first signs of physical breakdown, in order to be fully prepared to prevent or cure an ailment, the patient should be cared for as in a general hospital, where the menu is as much a part of the therapy as any of the physician's orders.

The use of new chemical preparations and medical supplements permit greater latitude when it comes to dietary observance. Control can be maintained of a patient who cannot tolerate strict or protracted dieting.

Nothing is intended to bend the Home to the service of capricious or eccentric demands. The dietary regime is for the benefit of the patient. When he chooses to depart, openly or covertly, from the menu established for all, this conduct, and the background from which it rises, must be recognized and understood. The Home should be prepared to have its health team take over and provide whatever medical assistance will be necessary. But the effort by the individual to express himself about food should not be disciplined.

Family Homes for the Aging.

RUTH L. GOLDBERG, *Caseworker, Jewish Family and Children's Service, Detroit.*

Basically this paper discusses from the casework point of view how the Jewish Family and Children's Service of Detroit uses private family homes, or as we refer to this, "Private Family Care," in its Department of Services to the Aging. The purpose of Private Family Care is to provide a comfortable substitute home for people 60 years of age and over with families other than their own.

The importance of an awareness of our own feelings regarding aging in general is pointed out. In working with the aging the caseworker gives full recognition to the view that both the adult children as well as the parents have the right to seek a life of their own and to decide for themselves how close the familial bond between them can be. Emphasis is placed on the fact that no matter what phase of life the individual is in, our basic concept of helping a client use himself most effectively within his particular situation applies as

much to work with the aging as with any other age group. The same basic casework techniques are utilized in working with the aging as with younger people. However, because of the nature of the aging process itself and the problems inherent in it, some supplementary techniques have been found useful and reference is made to these in the paper.

In the home-finding process, eligibility requirements for Private Family Care homes are discussed, as well as the responsibility the home owner has in relation to the aging person placed in the home and to the agency. The agency responsibility to each is clarified.

The meaning of placement is explored with the aging individual in order to determine whether this plan will meet his needs. Here, other community resources available are gone into and defined with him in order to give him every opportunity to make the choice that is right for him.

This paper goes into the various phases of placement using examples of actual case material. Private Family Care is a placement plan which affords the caseworker a real opportunity for constructive casework help. It enables the worker to help the client face realistically the amount of help he really needs and to utilize the actual positive strengths and elements of independence found in the very nature of Private Family Care, as compared to institutional care, which to older people often means complete dependence and subjugation.

It concludes with the fact that it becomes increasingly clear that in any phase of work with the aging we as caseworkers have a real responsibility in meeting the challenge of developing greater understanding of the needs of the aging and helping them toward healthier adjustment through casework service.

Factors Affecting the Selective Use of Social Clubs for Older People.

MARCELLE G. LEVY, *Council of Social Agencies, Syracuse.*

(Abstract not received.)

Improvement of State Programs: A Challenge to Gerontology.

MARY C. MULVEY, *Chairman, Rhode Island Committee on Aging, Provincetown.*

There are few who doubt the need for more competent personnel to handle the problems of the aging. A desirable plan is one in which an administrator at the State level, a generalist in gerontology, would take the lead in coordinating efforts of specialists in gerontology within their respective professions and in stimulating lay persons to participation in their communities.

The increase in numbers of State Committees on Aging has been one of the most significant developments in the field. As nominal head of aging programs, the committee through its staff is responsible for short- and long-range planning and aggressive and determined professional leadership. This leadership function is a distinct challenge and points up the need to formulate effective theories of administration, and, through practical measures, to find ways and means for the training and direction of personnel to work with the aged.

The challenge to gerontology in improving administrative objectives and techniques is an underlying theme. Gerontology is charged with setting criteria for forming effective State programs, for effective cooperation between State and other agencies and the communities at large, for preparing prospective personnel to assume leadership so that in the future more intensive efforts will be directed toward the communities for assuming responsibility. The discussion is theoretic and suggestive rather than factual and conclusive.

Individualized Care of the Aged.

G. H. REEVE, *Montefiore Home, Cleveland.*

(Abstract not received.)

Nutrition, A Factor in the Mental and Physical Health of Older People.

MILDRED REYNOLDS, *Professor of Home Economics, Purdue University, Lafayette, Indiana.*

It is well-established that nutrition, a major need of senior citizens as well as those of other groups, plays a vital role in physical and mental health. Malnutrition, whether in the form of under-nutrition or over-nutrition, leads to various physical disturbances and deterioration, to unhappiness, and to undesirable social attitudes.

Nutritionists and other professional personnel actively concerned with food for the senior citizen point out the important fact that a practical approach to the problem is needed. Essential nutrients, namely, protein, minerals, and vitamins, not only must be distributed in the daily diet in recommended amounts, but the foods containing these protective elements must fall within the customary food and economic patterns of the senior citizen. Furthermore, the carefully selected food must be well prepared so as to protect it against unnecessary loss of nutrients and to insure acceptance.

Residence groups, *e.g.*, Senior Centers, Nursing Homes, and Homes for the Aged may be so organized as to have the direct supervision of the food services by professional personnel, nutritionist or dietitian. When that is not the case, a consultant may, if requested, provide guidance in menu planning, food selection within the accepted dietary pattern and budget limits, correct methods of food preparation and service, and other problems of the department.

Senior citizens living in the family unit or alone may request individual consultant services, when available, or they may receive assistance through educational programs presented at senior citizen meetings. It is encouraging to observe that this plan has become a practice among many of the present diversified educational programs for senior citizens. These programs are being fortified by results of research that deals with various aspects of food and nutrition for people in middle and later life. Expansion of research activities in this field is recommended.

Socio-Medical Investigations for the Benefit of the Accommodation of the Aged.

R. J. VAN ZONNEVELD, *Coordinating Physician for Gerontological Research, National Health Research Council, T.V.O., The Hague, The Netherlands.*

In the Netherlands the number of old people exceeds 900 000 at the moment, being 8.5% of the total population. As there is an estimated shortage of 250,000 houses, the housing problem of the elderly is urgent.

Several smaller or larger surveys have taken place to try to assess the wishes and needs of various groups of the aged with regard to this point. An interview of 3,000 aged persons in Groningen and 5800 old people in Rotterdam revealed for instance their unwillingness, for the greater part, to move into an old-age home, even when this was considered better from a socio-medical point of view.

The number of persons in need of care or of nursing is of great importance for the planning of old-age homes and nursing-homes.

A small survey (Hornstra, 1953) on a South-Holland isle, estimated that 2% of the aged should be admitted into a nursing-home. The Groningen (Urban) survey (van Zonneveld, 1954) estimated this percentage at 3.2 (1.1% was considered in need of immediate admission into a nursing-home), while in the agricultural region of South-West Frisia Schreuder came to a percentage of 2.3-4.2. The survey in Rotterdam put the percentage for those in need of nursing (not necessarily in a special home) at 5.4, while that for general maintenance was about 22. In Groningen at least 3.7% of the aged should be admitted without delay into an old-age home, should their health conditions not worsen greatly. Though an exact comparison of the data is not justified, it can be considered that at least 2% of the aged are in need of a nursing-home. Various relevant data will illustrate the foregoing more in detail.

A Social Activities Center Evaluates Its Organizational Patterns and Methods of Work in Light of What It Has Learned about the Psycho-Social Needs of Older People.

FLORENCE E. VICKERY, *Executive Director, San Francisco Senior Center, San Francisco.*

If there is any one thing that characterizes the hundreds of social programs for older people that have developed in this country, it is their complete heterogeneity. They are called by different names, sponsored by various organizations, use many kinds of facilities, are financed in planned and unplanned ways, offer highly organized programs or simple unstructured activities with professional or volunteer leadership or no leadership at all. Uniformity in these projects is not possible or even desirable, since each is dependent on the resources of the individual communities in which they are located.

There is one aspect of these programs, however, on which we must soon achieve some common approach—that is, an educationally and psychologically sound philosophy about the importance of these programs and the contributions that they can make to the mental health and well-being of the individual participants. Such a philosophy for our work must be so clearly stated that it can be implemented with well-defined goals and objectives. To reach goals, one must have methods of work and our methods must be such as will measure up to standards that have been established for working with other age groups in informal education and social activity settings.

A sound philosophy for our work that can be clearly stated and implemented through realistic goals and objectives will determine what success we will have in three critical aspects of the development of these programs within the next decade.

First: What success we will have in attracting into this field qualified recreation and social group workers, not only to direct our established programs, but to supervise the training of additional professional workers.

Secondly: What success we will have in securing support from Foundations to undertake needed operational research.

Thirdly: What success we will have in securing from our communities sound, adequate, and permanent financing for our programs, either from public funds or from established community fund-raising efforts.

From the laboratories of our fellow gerontologists—the sociologist, physiologist, psychologist, and psychiatrist, well documented findings are available to us on the psycho-social needs of the human personality in the latter years of life and the stresses and changes which characterize these years. We will need to familiarize ourselves with these findings and use them in our planning if our programs are to be effective in helping older people to make some of the social and emotional adjustments that the latter years bring.

The paper will review some of the things we have learned about the needs, interests, and behavior of older people and the organizational patterns and methods of work that have been developed at the San Francisco Senior Center in light of these needs.

Techniques Involved in the Counseling and Placement of Older Workers.

P. A. WILSON, *Counselor for Older Workers, Vocational Guidance and Rehabilitation Services, Cleveland.*

The purpose of this paper is to point out the special applications of existing techniques involved in counseling older workers. By implication, the differences involved in this type of counseling as compared with that generally employed in dealing with young people will be apparent. Consideration will be given to the insecurity felt by older workers who are unemployed, their emotional stresses and strains, their need to share their life experiences with the counselor, and their need for reassurance, understanding, and sympathy. Attention is given also to the obstacles encountered in the counseling process, such as the need to readjust to a new type of work and the possibility that the client will have to accept a lower grade of work at a lesser rate of pay. The obstacles encountered by the counselor in attempting to place the individual will also be touched upon, and consideration will be given to the bearing of physical handicaps and chronic illness on the performance of specific tasks. In conclusion, mention will be made of types of work available to older men and women, and a number of successful case histories will be outlined.

Leisure-time Attitudes of Healthy Older Persons.

E. G. YOUMANS, *National Institute of Mental Health, Bethesda, Maryland.*

Social psychologic aging may be defined as the decreasing ability to find and perform satisfying roles. Preliminary findings in an investigation of 50 healthy, non-psychotic, non-institutionalized men age 65 and over who volunteered for study indicate that a sub-

stantial proportion have experienced very little social psychologic aging. Two-fifths expressed many varied and distant goals in their present roles and two-thirds registered enjoyment and moderate to strong identification with what they were doing. Over one-half showed an optimistic view toward the world in general, said they preferred to be their present age rather than younger, and maintained that the problems faced today were easier than problems faced in the past.

Those who received strong emotional support from their families, relatives, and friends, compared to those who were given weak emotional support, found more enjoyment in their leisure time, had a greater variety of immediate and distant goals, possessed a stronger identification with their activities, and expressed more positive feelings about retirement. On the other hand, forced retirement and losses of significant persons tended to increase negative attitudes toward leisure time. Occupational "success" was not significantly related to leisure time attitudes, and manual workers expressed more favorable attitudes toward Golden Age Clubs than did professional and white collar workers.

Technical Exhibits

Carnation Company, Los Angeles (Booth No. 26)

Carnation Company welcomes friends of long standing as well as new members of the Gerontological Society. At Booth No. 26 a refreshing drink of Carnation Instant Nonfat Milk will be served. Carnation representatives will be pleased to discuss with you the physician-researched material for use in your practice as a service of Carnation Company.

Doho Chemical Corporation, New York (Booth No. 25)

Doho Chemical Corporation is pleased to exhibit: Auralgan (ear medication in otitis media), Otosmosan (fungicide and bactericide in suppurative and aural dermatomycotic ears), Rhinalgan (nasal decongestant), and New Laryglan (soothing throat spray and gargle). Mallon Chemical Corporation, subsidiary of the Doho Chemical Corporation, is also featuring: Rectalgan (liquid topical anesthesia), and Dermoplast (aerosol freon propellent spray for relief of surface pain, itching, burns, and abrasions.

S. F. Durst & Company, Philadelphia (Booth No. 22)

At Booth No. 22, Durst will present two outstanding products of interest to any physician interested in Geriatrics: Senilex, a mental clarifier for the aged, which is designed to aid in senile mental deterioration, especially mild memory defects, confusion, and abnormal behavior; and Pedameth, oral therapy for the control of the odor arising from incontinence.

Organon, Inc., Orange, New Jersey (Booth No. 24)

Physicians are cordially invited to visit the Organon booth for information on the various Organon pharmaceutical specialties. Included among these are: Vistabolic, the new geriatric tonic; Cortrophin-Zinc, the long-acting aqueous ACTH; Liquaemin, America's first and purest heparin; Trevidal, the protective, balanced and controlled antacid; and Pernaemon, the painless U. S. P. liver extract. Organon representatives will be happy to discuss these advances in therapy with all interested physicians. Also available will be information on the new and complete systemic hemostat, Adrestat.

Reed & Carnrick, Jersey City, New Jersey (Booth No. 23)

Scientific Exhibits

Cleveland Health Museum, Cleveland.

The Convention and Visitors Bureau of the Chamber of Commerce of Greater Philadelphia, Phildelphia.

Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, Bethesda.

Brooklyn Hebrew Home & Hospital for the Aged, Brooklyn.

Division of Gerontology, University of Michigan.

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G. C. La Belle, Rome, N. Y.

H. G. Laue, Chicago

I. H. Leopold, Philadelphia

R. G. H. Leuchtenberger, Cleveland Heights

A. A. Lombardi, New York

M. Lorton, Belleville, Ill.

W. A. McDougall, Kansas City, Mo.

M. E. McKinney, Yonkers, N. Y.

H. C. Meng, Nashville

Mother M. de Lourdes, New York

C. J. Mount, Los Angeles

W. Posner, Bayside, N. Y.

J. Quintero Quintero, Caracas, Venezuela

H. Seidel, Baltimore

M. J. Shore, Brooklyn

H. R. Stark, San Marino, Calif.

J. H. Taterka

C. Tibbitts, Rockville, Md.

R. F. Tishman, New York

R. Villegas, Boston

J. Weil, Cleveland

E. L. Wenk, Shreveport

L. Wexler, New York

H. H. Zinsser, Los Angeles

B. Zufall, Forest Hills, N. Y.

INDEX TO CURRENT PERIODICAL LITERATURE

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National Institutes of Health

THE SUBJECT categories are those in *A Classified Bibliography of Gerontology and Geriatrics* by Nathan W. Shock published by Stanford University Press, Stanford, California (1951). Only major headings are used and the Roman numerals correspond to those given in the bibliography. In so far as possible, references are classified according to organ systems. Thus, most of the material on Geriatrics will be found under the organ system involved in the disease. Cross references are indicated by number at the end of each section. When available, abstract references are given (*B.A.—Biological Abstracts: P.A.—Psychological Abstracts,* and *P.I.—Population Index*). Abbreviations for journals are those used in *A World List of Scientific Periodicals Published* in the years 1900-1933, 2nd Edition. For journals not listed, abbreviations were devised according to the general rules used in the above source. It is impossible to cover all journals and list all papers concerned with aging and the aged. Authors and publishers are requested to call attention to publications or to send reprints to the Gerontology Branch, Baltimore City Hospitals, Baltimore 24, Maryland. The assistance of the Forest Park Foundation, Peoria, Illinois, in the preparation of these materials is gratefully acknowledged.

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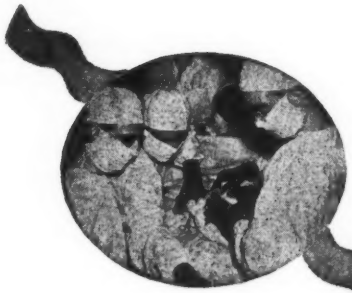

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